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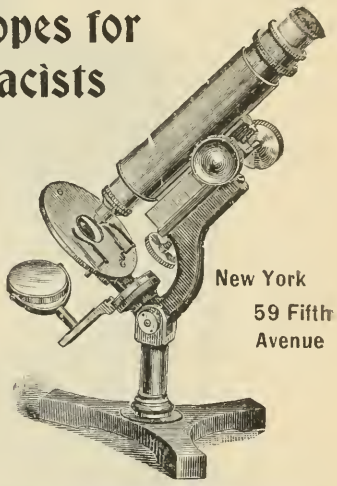

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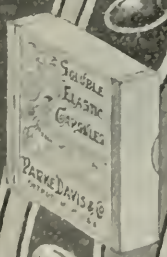

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THE AMERICAN
JOURNAL OF PHARMACY

NOVEMBER, 1901.

ADRENALIN THE ACTIVE PRINCIPLE OF THE SUPRARENAL GLANDS AND ITS MODE OF PREPARATION.

By Dr. Jokichi Takamine.

I have no doubt that a good many of you present have read an account of adrenalin, and some of you no doubt have used it. Inasmuch as, however, this is the first time the active principle of the suprarenal glands was isolated in a commercial scale, and such might lead to the isolation of the active principle of other interesting glands, I venture to submit before you a brief sketch as far as investigation has gone.

Forty-six years ago, Adison first observed the certain changes of the suprarenal glands and their relationships to the disease now bearing his name. Oliver and Schafer's work on the physiological action of the glandular extract, was soon followed by Scymonowicz, Cybulski, and later by many others. The suprarenal therapy has since become, not only a subject of scientific interest, but has successfully been applied in various branches of medical practice. Marvelous therapeutic value of the suprarenal extract has now been established and proved beyond all doubts.

As the use of suprarenal extract increased, a keen desire to obtain its active ingredient in pure state was generally felt by medical practitioners, for reasons that the said extract is prone to deteriorate very rapidly and hence the necessity of preparing fresh each time before use.

Many able chemists turned their attention toward isolation of the active principle, desiring it might become a very useful agent in therapeutics. So far as chemical nature is concerned, but a little

knowledge has been contributed over Vulpian's original observation that ferric chloride and iodine impart characteristic hues to the glandular juice.

J. J. Abel's investigation on the subject has no doubt thrown some light on the chemical side ; unfortunately for him, however, he was not working with the active principle but a somewhat modified substance, or the benzoyl-compound which withstood his autoclave treatment.

Otto von Furth, of Germany, worked on the same line of research and has already written several papers in which a controversy against Abel's epinephrin was entertained. Epinephrin is a substance in suprarenal glands isolated by Dr. Abel and claimed by him to be the active principle.

It is von Furth who declared that epinephrin is not the active principle of the gland but an inert substance mixed with diversified proportion of his suprarenin, which he claims to be the real principle, according to conditions of preparation, hence its variegation of physiological activity. Epinephrin may be made entirely inactive by simply refining it. This was also observed by Abel who ascribed its modification to the nature of the substance and concluded that there are at least two isomers of epinephrin, namely, active and inactive.

Suprarenin, according to its author, is obtained from the filtrate in which Abel considered no epinephrin does exist. The wide difference in the process of preparation and almost entire dissimilarity of chemical reaction of the suprarenin and epinephrin tends to put outsiders in obscurity in determining whether or not there are two ingredients in suprarenal glands, exerting similar physiological activity.

Abel, however, recently published a further observation on epinephrin, in March number of the Johns Hopkins Hospital Bulletin, 1901, in which he substantiated von Furth's statement that the unaltered or rather native active principle of the gland is not at all precipitable by ammonia and naturally he recognized that epinephrin was indeed a modified substance of the active principle as Furth argued, thus having partly concluded the dispute between the two authors. Still, however, there remains a question whether suprarenin be the pure active ingredient or a mixture thereof, with more or less inert matters, as long as von Furth cannot get it in pure, stable, definite forms.

Last summer I devoted my attention to this subject and am pleased to announce that I have succeeded in isolating the active principle in a pure, stable, crystalline form, the base itself. I do not by any means desire to usurp the credit due to the pioneer investigators, yet in view of the fact that neither of the authors quoted above have obtained the active principle in a pure form, and that there may exist some room for controversy, I have, therefore, termed my substance, as I isolated, "Adrenalin."

Isolation of the active principle of the suprarenal glands:—

The mode of preparing the active principle of the suprarenal glands is as follows: Suprarenal capsules finely disintegrated by suitable means, are steeped in water or acidulated water for a period of about five hours at a temperature varying from 50 to 80 degrees centigrade, with frequent agitation and with the addition of water as it evaporates. The temperature of the mass is now raised from 90 to 95 degrees centigrade for the period of one hour so as to coagulate as much albumenoid as possible.

As the active principle of the glands is prone to absorb the oxygen from the air, to form inactive substance, it is necessary to avoid exposure of the liquid to the air as much as possible. A layer of fat floating on the surface of the mass acts very conveniently for this purpose and at the same time it has an effect of retarding evaporation of water as well. Other methods of preventing oxidation may be employed at this stage, such as conducting the steeping process in an atmosphere of carbonic acid gas. The mass is now pressed and separated from the liquid portion which contains the active principle. The mass is again steeped for hours in warm water slightly acidulated with acetic or hydrochloric acid, in order to extract the residual amount of active principle. The liquid separated from the mass is now added to the first extract and allowed to separate from the oil. The clear extract is now evaporated in a vacuum pan to a suitable strength. To this concentrated solution about two to three times its own volume of strong ethyl alcohol is added, or more economically wood spirit, which will precipitate both inert organic and inorganic substances. The inert substances thus separated are washed with alcohol so as to free them from the active principle. The alcohol solution is now evaporated preferably in vacuum still, whereby the alcohol used is duly recovered. To the residual liquid, ammonia is now added until the

solution gets distinctly alkaline and left over for several hours. A yellow brownish precipitate will be formed which is the crude adrenalin in a basic form. The precipitate is now filtered, washed with water and dried. The impure adrenalin usually precipitates in a light yellow brownish tomato-shaped form, but not infrequently in needles. The former is an agglomeration of needle crystals and is more or less contaminated with coloring matters and some inorganic substance, chiefly phosphates.

Instead of using ammonia, sodium hydrate may be used as a precipitant, but care must be taken not to use in excess, which redissolves adrenalin. In order to counteract caustic alkali, ammonium chloride or carbonic acid may be conveniently used. In fact, the various modifications and combinations of these processes may be adopted.

For the further purification of the adrenalin, the crude adrenalin is dissolved in acid and alcohol and ether is added to a sufficient quantity. A brown colored precipitate is produced which chiefly consists of coloring matter and inorganic impurities. The precipitate is separated both by decantation and filtration. The filtrate is now treated by one of the above-mentioned processes, when white crystalline precipitate of adrenalin will be obtained. It is quickly filtered, washed with water and then with alcohol and dried. The process of purification may be repeated, if desired, two or three times.

Properties and Deportments:—

Adrenalin is a light white, micro-crystalline substance, having, so far, observed to separate in five different forms of crystals according to the condition of solutions from which they be crystallized: 1. Prisms; 2. Fine needles; 3. Rhombic plates; 4. Boat or leaf-shaped; 5. Wart like.

Adrenalin has a slightly bitter taste and leaves a numb feeling on the tongue where it has been applied. In dry form it is perfectly stable. Adrenalin shows weak alkaline reaction on moistened litmus paper. Phenolphtalein also indicates slight alkalinity. It is soluble with difficulty in cold water and more readily in hot water. From the hot saturated aqueous solution the crystals separate on cooling. The colorless aqueous solution of adrenalin is prone to oxidation, absorbing oxygen from air and assuming colors from beautiful pink to red and eventually brown. It is easily soluble in

acids, and alkali hydroxides, forming salts. Ammonia and alkali carbonate do not dissolve adrenalin. Adrenalin solution made alkaline with alkali hydroxides and carbonates as well as alkaline earth hydroxides, readily absorbs oxygen from air, its rapidity being exactly proportionate to the strength of alkalinity.

The following are some of the characteristic reactions: Ferric chloride colors adrenalin solution emerald green, while iodine imparts a vivid pink, as first observed by Vulpian. A careful addition of caustic alkali to the green solution colored by ferric chloride, gives rise to the various shades of hue ranging from purple to carmine red, which is destroyed by careful neutralization with acids, restoring its original color. Oxydizing agents such as nitric acid, potassium bichromate and ferricyanide, etc., behave in a similar manner as iodine does. Gold chloride is very energetically reduced by adrenalin and a complete separation of the metal follows, from acid solution, by application of gentle heat; resultant liquid is colored pink or carmine red according to the strength of the solution used, as is the case with different oxydizing agents.

None of the following alkaloidal reagents produce precipitation: Mercuro-potassium iodide, picric acid, tannic acid, phosphomolybdic acid, phospho-tungstic acid, mercuric chloride, lead acetate, potassium bichromate and platinum chloride.

Analyses of Adrenalin:—

Combustions of adrenalin had been made in my laboratory and the following results were obtained:—

	I.	II.	III.	IV.	Average.
C	59·54	59·33	59·40	59·28	59·38
H	7·99	8·13	7·62	7·62	7·84
N	8·40[1]	8·13	7·74	7·76	7.88
O					24.94
					100.00

The probable empirical formula of adrenalin, calculated out of the above figures as basis, is $C_{10}H_{15}NO_3$.

100 parts of adrenalin needs nearly 19 parts of hydrochloric acid in forming a neutral salt and this substantiates the approximity of correctness of the formula, for 100 parts of the substance requires, by calculation, exactly 18·5 parts of HCl.

[1] The figure of N under No. I, was roughly estimated by the Kjeldahl method with the intention of having an approximate amount of nitrogen and therefore may not be regarded as accurate.

T. B. Aldrich, of Detroit, reported in his paper (August number of the *American Journal of Physiology*) that he had also succeeded in the isolation of the crystalline active principle of the suprarenal glands by the use of basic acetate of lead as a precipitant, and later by ammonia. He proved by analysis that his substance was exactly identical with my adrenalin.

Aldrich's formula is $C_9H_{13}NO_3$, which differs with mine by less CH_2. Aldrich observes that "if we subtract a benzoyl residue C_7H_5O from Abel's formula for epinephrin ($C_{17}H_{15}NO_4$) we obtain $C_{10}H_{10}NO_3$," which is not very far from Aldrich's own result.

It will be of some interest to arrange tabularly the empirical formulas of the glandular active principle, according to the results and claims by different authors:

Furth.	Abel.	Aldrich.	Takamine.
$C_5H_7NO_2$	$C_{17}H_{15}NO_4$	$C_9H_{13}NO_3$	$C_{10}H_{15}NO_3$

or

$C_5H_9NO_2$.

The further investigations on different chemical behaviors of adrenalin will help to determine the correct formula for this interesting product.

Salts: Adrenalin is very soluble in acids and alkalies, and forms its salts which are not crystallizable. I made three kinds of salts—hydrochloride, sulphate and benzoate—by carefully dissolving adrenalin with the acids respectively and evaporating in vacuo over strong sulphuric acid. In the long course of time they all became dark brown, brittle masses, deliquescent in the air. So far my efforts to crystallize them have failed.

Alkali compounds are easily affected by oxygen of air and their crystallization is entirely impossible.

Benzoyl Compounds: Pure adrenalin is dissolved in a slight excess of an alkali solution, in a separating funnel, and benzoyl chloride is gradually added, shaking the contents briskly after each addition. After shaking a quarter or half an hour a yellow-brownish oily liquid will settle on the bottom of the funnel, and supernatant liquid will be found suspending some crystalline substance, and reacts no longer with ferric chloride, after acidulating with hydrochloric acid, showing that adrenalin has entirely combined with benzoyl by the manipulation. The oily liquid is first washed with water, and then with a diluted sodium carbonate solution, followed

with repeated washing with cold water until it is no longer alkaline. This oily substance had been kept over several months, still it showed no signs of crystallization but dried up to a transparent amber colored brittle mass.

I have tried it with different solvents in view of crystallizing but thus far in vain, and concluded that this portion of the benzoyl compounds is not crystallizable.

The other portion of the benzoyl compounds is crystalline, but without any defined form, and dissolves very easily in ether and alcohol, from which solution again the similarly formed substance can be obtained by evaporation of either alcohol or ether.

Analyses of both compounds are not yet finished on account of lack of pure substance, but I hope I will be able to report before long.

Action of Potassium Hydroxide on Adrenalin: To caustic potash, fused in a silver dish at as low temperature as possible, adrenalin (about one-quarter in weight) is carefully added when the mass will swell up, emitting noxious odor which partly has the smell recalling homologous pyridins. As soon as the swelling subsides and the mass uniformly fuses, the dish is removed from fire and cooled and then dissolved in water. This aqueous solution is now shaken with ether which takes up a substance which discharges a peculiar penetrating odor of indol or skatol, but substance is in such a small quantity that prohibits further manipulations for chemical proof. I think it is proper to attribute this production of skatol or indol smelling substance to the contamination of albuminous matters which is practically unavoidable in case of crude adrenalin.

The portion separated from ether is acidulated with hydrochloric acid and again shaken with ether which leaves beautiful needle crystals on evaporation. These crystals are the mixture of two substances with almost similar reaction toward ferric chloride. On determining the melting point of the crystals respectively, it was found that one melts at about 100° C. while the other melts at about 190° C. Both are easily soluble in water as well as in alcohol. Ferric chloride colors the solution of the crystals a beautiful emerald green which turns red by careful addition of sodium carbonate solution. Silver nitrate and Fehling's solution are reduced by them and lead acetate produces a voluminous precipitate.

I could not obtain enough quantity of both crystals, so as they

can be subjected to analyses; but as far as their chemical reactions and melting points are concerned there is little doubt to believe that the mixture consists of protocatechuic acid and pyrocatechin. The former is easily changed to the latter while the fusion is going on. Surmising chief production by the potash fusion be protocatechuic acid, it may be possibly right to conclude that in adrenalin molecule there is such a residue, $C_6H_3(OH)_2$—as is linking to the other residue $C_4H_{10}NO$. I cannot at present furnish chemical proof for the above supposition but hope to continue further investigation during this winter, when the material can be obtained and manipulated without any fear of deterioration, and report on the results.

Physiological Properties: The physiological activity of adrenalin thus isolated is astoundingly strong. A fraction of one drop of aqueous solution of adrenalin or its salt in strength of 1 : 50,000 blanches the normal conjunctiva within one minute. It is the strongest hemostatic agent known.

The intravenous injection of adrenalin produced a powerful action upon the muscular system in general, but especially upon the muscular wall of the blood vessels and the muscular walls of the heart, resulting in an enormous rise of blood pressure. The result of three intravenous injections of 1 c.c. of the solution of adrenalin chloride of 1 : 100,000 into a dog weighing 8 kilograms raised the blood pressure corresponding 30 millimeters of mercury.

The above result, as well as other experiments, indicates that adrenalin is over one thousand times stronger than the fresh glands.

The therapeutic applications of adrenalin are already numerous and new uses for it are constantly found by investigators. Generally speaking, adrenalin when locally applied is the most powerful astringent and hemostatic known. It is useful in all forms of inflammation and is the strongest stimulant of the heart. It is non-irritating, non-poisonous, non-cumulative and without injurious properties. It has been used with good results as an antidote in morphin and opium poisoning, in circulatory failure, in the prevention of collapse in anesthesia, and in allied conditions. It is invaluable in carrying out bloodless operations in nose, eye, ear and throat work. It has also given good results in some cases of deafness, hay fever, nasal hemorrhage and various forms of heart disease. Such authorities as Doctors Mayer, Wilson, Bates, Reichert, Ingals, Stucky, Chambers, Curtis, Swain and many others have reported very favorable results.

The therapeutic efficacy of adrenalin has already been established beyond doubt, and it will unquestionably obtain a prominent place in the materia medica.

There are several useful applications of adrenalin in arts and industry; for instance, a developer of photographic plates, as a reducing agent in chemical analysis, art of dyeing, etc.

In concluding this paper, I desire to state that my thanks are due to Dr. E. M. Houghton, of Detroit, for making the physiological test, and also my thanks and large share of credit are due to Mr. Wooyenaka, my associate, for his energetic and able assistance in accomplishing this interesting investigation.

THE PHARMACOLOGIC ASSAY OF PREPARATIONS OF THE SUPRARENAL GLANDS.[1]

By E. M. Houghton, M.D.

Since Adison, in 1855, called attention to the relation of pathological lesions of the suprarenal glands to the disease which has since borne his name, these bodies have been the subject of numerous researches by workers in all lines of medical science. The histologist, the chemist, the physiologist and pharmacologist has each contributed his share to the sum total of the results obtained, which, often enough, have been widely divergent. But it is not my purpose to review the history of this interesting subject. It may be remarked, however, that for the first forty years the active principle found in these glands was the plaything of science, then leaped into prominence when Bates discovered that it could be employed as an astringent in ophthalmology, since which time physicians are finding new uses for it almost daily. In the course of some experimental work on the pharmacology of the adrenals, it appeared possible to take advantage of the marvelous influence of the active principle contained in extracts of these bodies upon the blood pressure which had been observed by Oliver and Shafer as a means of measuring their activity. Furthermore, it seemed quite advisable, as we had no chemical means of standardizing them, that some method of assay should be found, since in all probability in keeping with products of similar nature there must be much variation in the

[1] Presented at the St. Louis meeting of the American Pharmaceutical Association, September, 1901.

pharmacologic activity, owing to the liability to undergo chemical or bacteriological decomposition before, during, or after manufacture, in the various products that were to be obtained on the market.

Believing that the results of my observations may be of some interest to members of the Association, I will briefly outline the method that has given me the best results. This method is based upon the changes produced in the blood pressure of the carotid artery when variable quantities of a given preparation of the suprarenal glands dissolved in slightly acidulated water, the inert substance being removed as far as possible, are injected into the femoral, or jugular vein, of an anaesthetized dog or other animal.

The apparatus required are an operating table suitable for experi-

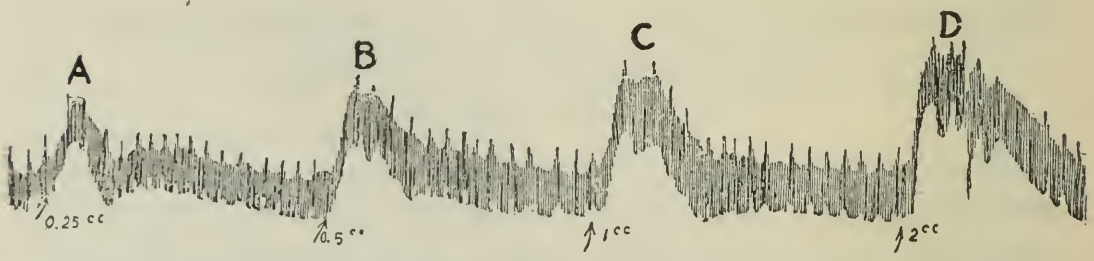

Fig. 1.—Blood-pressure tracing taken from the carotid artery of a dog anesthetized with chloretone. Suprarenal liquid diluted with normal saline solution to 5 c.c. in each instance was slowly injected into the femoral vein.

When injected into the circulation the principle of the suprarenal gland causes a marked temporary rise in the blood-pressure. The height of the waves in the above tracing (indicating the amount of pressure in the carotid artery) is directly proportionate to the quantity of adrenalin injected in each instance. For example, at *A* is shown the effect of the administration of 0·25 c.c. of suprarenal liquid; at *B*, of 0·5 c.c.; at *C*, of 1 c.c.; and at *D*, of 2 c.c

menting on dogs, and such surgical instruments as are usually found in physiological and pharmacological laboratories, including small glass conulae, suitable for inserting in blood-vessels and veins and a syringe of 10 c.c. capacity. A large-sized kymograph, with manometer arranged for taking blood-pressure tracings on continuous rolls of white paper, with ink pens, or fitted with the more convenient smoked-paper sheets, upon which the results are traced with a stylus is required. In either case, whether smoked or unsmoked paper is employed, for convenience in making measurements of the height of the blood-pressure tracings, the paper should have linear rulings, five millimeters apart.

The method is as follows: A small or medium-sized dog is care-

fully anaesthetized with chloroform, ether or chloretone. I have used the latter drug almost entirely, as but one dose, which is given per stomach, is required. In from fifteen to thirty minutes the animal is thoroughly anaesthetized, and will remain entirely insensible to pain for any length of time. Another decided advantage possessed by this anesthetic over chloroform and ether for laboratory work is the fact that the blood-pressure remains constant for many hours. After the animal is completely anaesthetized he is placed on the operating table, and glass conulae of suitable size are tied, as quickly as possible, into the carotid artery and femoral vein, the vessels being clamped off previously with forceps. The conula in the artery is connected to an inelastic tube, completely filled with a half-saturated sodium carbonate solution to prevent the blood from clotting by means of a short piece of rubber tubing, great care

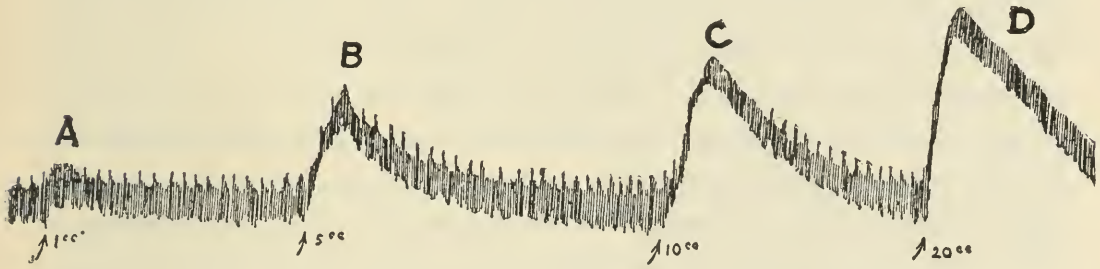

Fig. 2.—Blood-pressure tracing obtained in the same manner as No. 1. Suprarenal liquid solution was, however, more dilute than that employed in No. 1.

being exercised to exclude all air. The other end of the inelastic tube terminates in a U-shaped glass manometer tube which is partly filled with mercury, which has resting upon its free surface a glass float tipped with a glass writing pen or stylus. As soon as all the connections are made between the artery and manometer, the clamp employed to prevent the flowing of blood from the vessel is removed and immediately the float bearing the writing instrument begins to rise and fall in unison with the beats of the heart. The recording drum, which has been carefully placed in contact with the writing instrument, is released at the same moment and a graphic record of the blood-pressure and heart beats is made upon the traveling sheet of paper. A few inches of record are taken as a normal tracing. Then a quantity of the solution of the preparation of the suprarenal glands, representing a known quantity of the product, is injected into the vein, through the other glass cornula, care being

again exercised to prevent the entrance of air into the vessel. Within a few moments after the injection the blood-pressure is enormously increased, but it quickly falls again to the normal. As soon as the blood-pressure has become normal a second injection is made in precisely the same manner, of a known quantity of the standard solution of the suprarenal gland. Again increased blood-pressure results. A comparison of first and second tracings will show whether more or less of the solution being assayed should be injected to produce the same rise in blood pressure as is produced by a given amount of the standard preparation. Ultimately, by repeating the injections, the requisite amount of the preparation being assayed will be found which will produce a rise in blood-pressure equal to that produced by a given quantity of the standard. The extent of the rise in blood-pressure varies in proportion to the amount of the active constituent of the suprarenal gland injected. Several dogs are usually required for making an assay. Two kinds of tracings may be made. Complete when the drum of the kymograph is allowed to run continuously, and abbreviated when the drum remains stationary, while the reaction takes place. In the latter the rise in blood-pressure is recorded as a short, perpendicular line. These abbreviated tracings answer admirably for most work, as only variations in blood-pressure are taken into account. The smoked paper tracings are fixed by dipping them into shellac, and allowing them to dry. A great many precautions must be observed in carrying out the experiments, such as the amount of material injected at one time, since the extent of the increase in blood-pressure must be sub-maximal, the volume of fluid injected at one time, the length of time required in making the injections, etc., but in keeping with all other methods of pharmacologic assay the conditions obtaining in the experiments must be kept constant and the reaction of the preparation being assayed must be compared with a known standard.

Naturally the question will arise as to what should be the standard. At first a freshly prepared fluid extract of fresh bovine suprarenal glands was employed as a standard, but after the isolation of the active constituent, adrenalin, I adopted it as a standard, because its activity remains constant while other preparations of the suprarenal glands are prone to undergo decomposition, and consequent alteration in strength. The animals, after the experiments are concluded,

are immediately killed. Since the dogs are procured from the pound, and killed by an anesthetic instead of drowned, there should be no trouble with the humane societies.

The accuracy of the results obtained by the application of this method depend, like those of quantitative methods, generally upon the skill of the operator and attention to details. As a specific example of the results that may be obtained, the following illustration will suffice: Three samples of adrenalin, of known but concealed strength, were prepared and assayed. Calling the standard 100 per cent., the unknowns contained 40, 85, and 130 per cent., respectively. The results reported were 40, 83, and 135 per cent.

DIGESTIVE FERMENTS IN SURGICAL PRACTICE.

WITH THE FORMULA OF A PEPSIN SOLUTION, USED AT THE GERMAN HOSPITAL, PHILADELPHIA.

By M. I. Wilbert.

The local application of digestive ferments, to dissolve the coagula and putrescent matter found in lesions, or the products of morbid changes in the living human organism, is not new. Especially is this true of the vegetable ferment derived from a South American species of papaw. The proprietary preparations made from the milky exudation of this plant have been recommended, and used quite extensively, to dissolve the false membrane in cases of diphtheria. This same class of preparations has also been used to some extent for external application, to aid in cleaning out disagreeable sloughing ulcers, by dissolving the broken down granulations and albuminous exudate that offer both shelter and food for colonies of micro-organisms.

The latter use of this vegetable ferment is evidently a very old one, and borrowed from the practices of savage or semi-savage races. Mr. F. B. Kilmer in "The Story of the Papaw," published in recent numbers of The American Journal of Pharmacy, relates how the native South American doctors use a paste, made up with the juice of the papaw, as one of its chief ingredients, as a dressing for foul ulcers and offensive sores that occur among the natives in hot climates.

While this vegetable ferment has the decided advantage of being active in either an acid, neutral or alkaline medium, and, theoret-

ically at least, should have a very wide field of usefulness, nevertheless it has several disadvantages that are quite a drawback to its general adoption in surgical, or even medical practice. One is the very high price demanded for the different commercial preparations. Another is the variation that exists in the digestive powers, of the different preparations on the market, and even among different samples of the same brand. And, in addition to this, we have no satisfactory way of making a fluid preparation of this drug that will offer any reasonable assurance of retaining the active principle of the drug unimpaired.

The animal digestive ferments have been so improved during the past twenty years through the scientific study of their physiological and chemical properties, and by improvements in methods of manufacture, that the proteolytic powers of pepsin for instance has been raised from 1·29 to 1·3000 and, according to the statements of some manufacturers, a pepsin having the power of digesting 15000 times its weight of coagulated egg albumen is not only possible, but is actually an article of trade at the present time. This improvement in the quality of these ferments would appear to open many interesting possibilities for their use, that as yet are not fully developed. If we remember the factors that are necessary for the digestion of albuminous proteids by the peptonizing enzyme we find that all the necessary conditions can readily be secured in a wound, ulcer or abscess of the living human body, and there need be little wonder therefore that the manufacturers of animal digestive ferments appear to have recognized the possible advantages to both patient and surgeon, that are to be obtained from the use of a peptonizing enzyme, as a physiological solvent for cleaning out abscesses, indolent ulcers and necrotic areas. And several more or less efficient preparations, put up especially for external application, are on the market at the present time.

It will readily appeal to all that a solvent that will attack and destroy necrotic tissues, without injuring the surrounding healthy cells, offers distinct advantages over corrosive or poisonous antiseptics, or caustic washes that at best only tear away or remove the superficial layers of dead cells, or if they do work down into the deeper tissues, poison and destroy many of the healthy living cells, and in this way accomplish more harm than good.

For the same reasons such a physiological solvent would appear

to offer many advantages over the use of the curette, for, while it is practically impossible to remove all the debris from a wound by mechanical means, without injuring and scraping away much of the healthy tissue, we can, by means of digestive ferment, remove all foreign or dead material, without injuring the vitality of the surrounding living cells, but, what is of more importance, it can be done without causing any appreciable amount of pain or discomfort.

A pepsin solution that has some resemblance to at least one of the commercial preparations, has been in use in the out-patient department of the German Hospital for some time, and appears to be giving very good satisfaction.

Mixed with two or three times its volume of water, and applied as a wet dressing, it has given excellent results by removing the broken down granulations and other septic materials from old chronic ulcers and abscesses, leaving a healthy granulating surface that may be treated as a clean wound in the regular way.

Following up our practice of giving a descriptive title or name to preparations having distinctive characteristics, we have christened this particular solution "Physol," this being a combination of the first syllables of the two words "Physiological Solvent" that describe better than lengthy phrases what the solution is really intended for, and what it will do.

The formula for this preparation, as used by us, is as follows.

	Grammes.
Pepsin (U.S.P.)	50·
Menthol	0·5
Eucalyptol	0·5
Oil of wintergreen	0·5
Alcohol	10·
Glycerin	50·
Diluted hydrochloric acid	20·
Talcum	50·
Distilled water to make	1000.

Dissolve the pepsin in 800 c.c. of distilled water, add the diluted acid and the glycerin, then dissolve the menthol, eucalyptol and oil of wintergreen in the alcohol and add this solution to the pepsin mixture. Add sufficient water to make the volume of the solution 1000 c.c., add the talcum and shake thoroughly, then filter through paper, returning the first portions until the filtrate runs perfectly clear.

The resulting solution is a clear, light yellow and pleasantly aromatic solution that appears to keep, without any appreciable change in its peptonizing properties.

THE ANATOMY OF THE FRUIT OF COCOS NUCIFERA.[1]

By A. L. Winton.[2]

(Contribution from The Connecticut Agricultural Experiment Station, New Haven, Conn.)

I. MORPHOLOGY AND MACROSCOPIC STRUCTURE.

Since the general structure of the cocoanut fruit has been treated by numerous writers on systematic and economic botany, only such facts are here given as are essential for a clear understanding of the relation of the parts and the microscopic structure.

The flowers are arranged in spikes branching from a central axis and inclosed within a tough spathe usually a meter or more in length (*Fig. 1*). A single female flower is borne near the base of each lateral axis, and numerous male flowers are distributed on all sides of the axis between the female flower and the apex. After the male flowers drop, each naked lateral axis persists and is a prominent appendage of the fruit (*Figs. 2* and *3 S*). Only one ovule of the three-celled ovary comes to maturity, but the tricarpelary nature of the fruit is indicated by its triangular shape as well as by the longitudinal ridges and the three eyes or germinating hole of the nut.

The epicarp of the fruit (*Fig. 3, Epi*) is a smooth tough coat, of a brownish or grayish color.

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[1] Reprinted from *The American Journal of Science*, Vol. xii, October, 1901.

[2] European microscopists have studied the foods and adulterants which have come under their observation but have overlooked a number of distinctly American products. The writer has undertaken to fill in some of these gaps by a series of papers, of which this is the second. The first paper, on the anatomy of maize cob, was published in the *Oesterreichische Chemiker-Zeitung*, 1900, p. 345, and also in the Conn. Experiment Station Report, 1900, p. 186.

Each paper will describe from the purely scientific standpoint the macroscopic and histological structure of the material investigated, and also in a final chapter point out the application of this knowledge to the detection of adulteration. The last chapter is not strictly suited to the pages of this Journal, but is so dependent on the scientific descriptions which precede it that it would be almost valueless if published separately.

FIG. 1. Infloresence of the cocoanut showing spathe inclosing the spikes each with numerous male flowers above and a single female flower near the base. × $\frac{1}{5}$.

FIG. 2. Half grown cocoanut fruit with calyx, and axis from which the male flowers have fallen. × $\frac{1}{5}$.

FIG. 4. Inner surface of a cocoanut shell with adhering outer testa. At the left the raphe, from which proceed veins forming a network over the surface. × $\frac{1}{5}$.

The mesocarp (*Fig. 3, Mes*), consists of a hard outer coat but a few millimetres thick and a soft portion, usually 3–4 c.m. thick, on the sides and much thicker on the base. Imbedded in the mesocarp are numerous longitudinally arranged fibers, varying in size from slender hairs to large, sparingly branching and anastomosing, flattened forms, 2–3 m.m. broad. The large fibers are situated chiefly in the inner layers, with their flat surfaces parallel with the surface of the nut.

Oftentimes the inner layers of the mesocarp become impregnated with a brown fluid, which on drying, gives the thin tissue a mottled brown appearance.

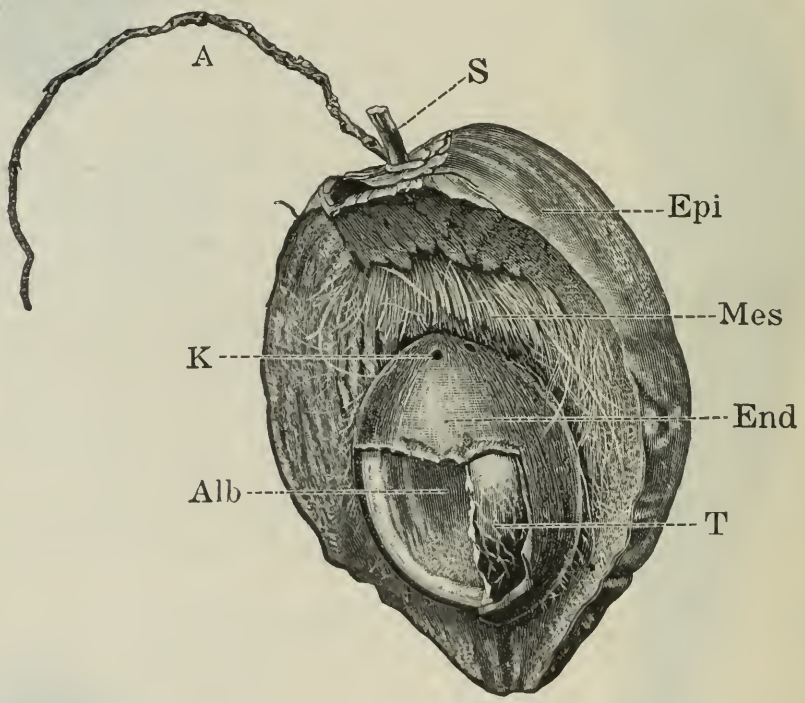

FIG. 3. Ripe cocoanut fruit. *S*, lower part of axis forming the stem; *A*, upper end of axis with scars of male flowers; *Epi*, epicarp; *Mes*, mesocarp with fibers; *End*, endocarp or hard shell; *T*, portion of testa adhering to endosperm; *Alb*, endosperm surrounding cavity of the nut; *K*, germinating eye. × ⅕.

The endocarp, or shell (*Fig. 3, End*), consists of a hard, dark brown coat, 2–6 m.m. thick, with numerous fibers adhering to the surface. Three nearly equidistant ridges (often indistinct) pass from base to apex, where they unite to form a blunt point. At the basal end, between the ridges, are the three depressions or eyes, the tissues of which are much softer and thinner than of the rest of the shell (*Fig. 3, K*). Through the softest of these eyes the embryo,

embedded in the endosperm directly behind it, escapes in sprouting.

The testa of the anatropous seed (*Fig. 3, T,* and *Fig. 4*) is a thin coat of a light brown color, closely united with the endocarp without and the endosperm within. Embedded in the outer portion and extending from the principal eye nearly to the apex is the raphe, consisting of a thin band of vascular tissues about 1 c.m. broad, which sends off branches in all directions, forming a network about the seed. The endosperm with the inner portion of the testa may be separated from the outer testa and endocarp by introducing a knife blade between the layers. By this operation the veins are split, part of the vascular tissue adhering to the convex surface of the inner testa, and the remainder to the concave surface of the outer testa, so that both surfaces are covered with reticulations.

The endosperm or meat of the cocoanut (*Fig. 3, Alb.*) is a white, fleshy layer, 1–2 c.m. thick, in which, near the base, is embedded the small embryo. While immature, the nut is filled with a milky liquid and has no solid endosperm, but as the ripening proceeds the endosperm is gradually formed and at the same time the milky liquid diminishes in quantity or entirely disappears.

Cocoanuts yield food for man and cattle, oil, fiber, and other useful products. The epicarp and mesocarp are cut away from nuts designed for export, although invariably a small amount of the mesocarp with its fibers remains attached to the shell. In removing the meat, the outer testa, as has been stated, also adheres to the hard shell, so that cocoanut shells consist not merely of endocarp, but also of a certain amount of mesocarp and testa.

II. HISTOLOGY.

The microscopic structure of the cocoanut seed is described by Hanausek,[1] Harz,[2] Moeller,[3] Koenig[4] and other authorities on foods and applied microscopy.

Cocoanut fiber (coir), which has long been extensively employed

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[1] *Die Nahrungs- und Genussmittel aus dem Pflanzenreiche*, Kassel, 1884, p. 155.

[2] *Landwirthschaftliche Samenkunde*, Berlin, 1885, p. 1120.

[3] *Mikroscopie der Nahrungs- und Genussmittel aus dem Pflanzenreiche*, Berlin, 1886, p. 241.

[4] *Die Untersuchung landwirtschaftlich u. gewerblich wichtiger Stoffe*, Berlin, 1898, p. 291.

in making mats and cordage, and also cocoanut shell, which has been used for making knobs and other turned articles, were studied by Wiesner[1] nearly thirty years ago, but his work was designed chiefly to distinguish the fiber from other commercial fibers and the shell from the similar shell of *Attalea funifera.*

Von Hoehnel[2] describes briefly the histology of coir, but, like Wiesner, does not appear to have understood the true nature of the stegmata.

Weiss,[3] Engler and Prantl,[4] and some other authors refer briefly to the microscopic structure of parts of the cocoanut, but their descriptions are of little value in diagnosis.

1. *Epicarp.*

The epicarp or epidermal layer is about ·015 m.m. thick and is made up of tabular cells with dark brown contents. In surface view the cells are usually square, rectangular or triangular, with double walls about ·005 m.m. thick and are arranged with some regularity in rows.

2. *Mesocarp.*

(*a*) *Hard ground tissue.*—This tissue consists of thick-walled cells which are often tangentially-transversely elongated. In the first few layers the walls are about the same thickness as in the epidermis, without evident pores, but further inward they are more strongly thickened (double walls often ·015 m.m. thick) and conspicuously porous. Still further inward they pass into the parenchyma of the soft ground tissue.

(*b*) *Bast-fiber bundles.*—In the hard ground tissue the bundles have no phloem or xylem but are composed entirely of bast-fibers with cell walls often thicker than the lumen. The number of fibers seen in cross section varies from two or three up to a hundred or more. Transitional forms between fibrous and fibro-vascular bundles occur further inward.

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[1] *Die Rohstoffe des Pflanzen-Reiches*, Leipzig, 1873, pp. 436 and 789. (A new edition is being published in parts, but the chapters on the cocoanut have not yet appeared.)

[2] *Die Microscopie der technisch verwendeten Faserstoffe*, Leipzig, 1887, p. 52.

[3] *Anatomie der Pflanzen*, Wien, 1878, 1 Band.

[4] *Die natürlichen Pflanzenfamilien*, II Theil, 3 Abteilung, p. 22.

(*c*) *Soft ground tissue.*—The thin-walled parenchyma cells of the soft ground tissue are in some parts isodiametric, in other parts longitudinally elongated, and in still other parts transversely-tangentially elongated (*Fig. 8, w*). Wherever the brown liquid previously referred to has penetrated the inner layers of the mesocarp, groups of the parenchyma cells here and there, being impregnated with this material, are of a rich brown color and appear thicker-walled than the others (*Fig. 8, br.*). This brown substance is quickly changed to a reddish color by caustic potash, but is not affected by alcohol, ether or the specific reagents for proteids, fats and resins. No immediate effect is produced by ferric chloride solution, but on long standing the color is changed to olive green.

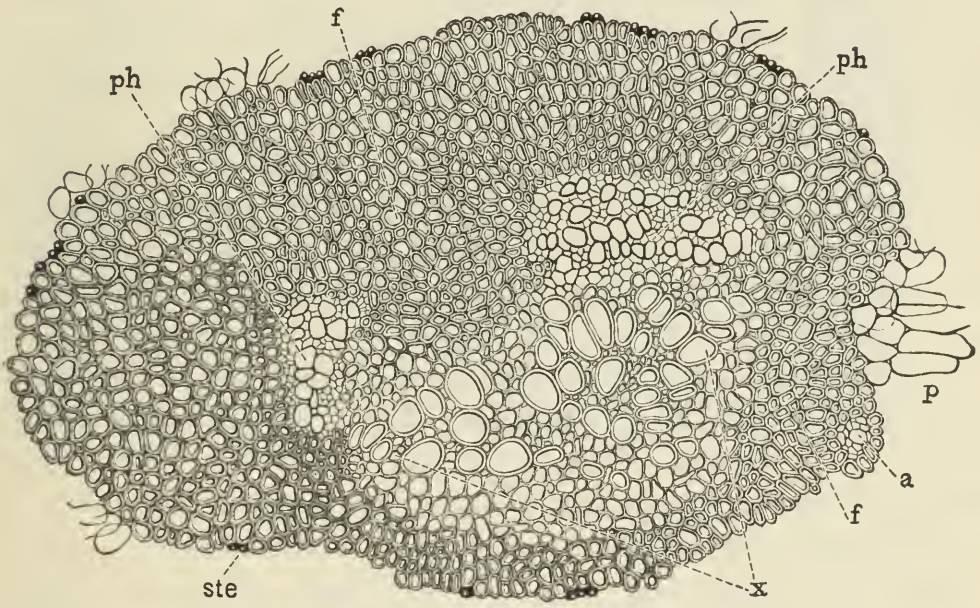

FIG. 5. Transverse section of a large flattened (mesocarp) fiber of the cocoanut. *ste*, stegmata ; *f*, sheath of bast fibers ; *ph*, two phloem groups ; *x*, xylem ; *p*, parenchyma of ground tissue ; *a*, rudimentary bundle belonging to small branch. × 90.

(*d*) *Fibers* (*Coir*).—These are fibro-vascular bundles with a strongly developed sheath of bast-fibers. Toward the xylem side of the bundle, particularly in the large fibers, the sheath usually diminishes in thickness and the vascular portion, as seen in cross section, is more or less eccentric, surrounded by a crescent-shaped sheath with the horns connected by a narrower strip.

In the smaller fibers there is but one group of phloem elements, but in the larger flattened fibers there are usually two, or occa-

sionally more, groups separated from each other by a continuation of the sheath (*Fig. 5*). Normally the xylem is near the inner flat side and the two phloem groups are approximately symmetrical with reference to the shorter axis of the elliptical cross section; but often the xylem is near one of the narrow sides and the phloem groups are symmetrical with reference to the longer axis, and still more often the arrangement is diagonal or otherwise irregular.

Mohl[1] in 1831 noted that the phloem in the stem of *Calamus* was normally divided into two distinct groups, and Kny[2] as well as other authors have since found the same arrangement in a number of palms. By the study of many sections, the writer has demonstrated that a cocoanut fiber with two phloem groups has also a double xylem, although in most sections no separation is evident, and the whole fiber consists of two simple bundles united side by side, which may completely separate further on in their course by the forking of the fiber.

Serial sections cut through such compound fibers show that at the place of forking the phloem groups are still further separated and the xylem also is divided by bast-fibers, thus forming two distinct bundles which pass into the two branches. The phloem in each branch is at first entire, but further on, if the branch is large it usually divides, and still further on the whole bundle may split up, with the formation again of two fibers. Occasionally a fiber which has no evident division of the xylem has four groups indicating that the fiber is composed of four united bundles, which, on branching, form two fibers each with a double bundle.

Large fibers not only fork but also send off small lateral branches. The rudimentary bundles belonging to such branches may often be seen in cross sections of the trunk fiber below the place of branching (*Fig. 5, a*).

a. Stegmata (*Figs. 5* and *6, ste*).—As seen in surface view these are circular or elliptical cells from ·008 to ·020 m.m. in diameter, which extend in longitudinal rows over the surface of the fibers. Longitudinal sections show that the cells are biconvex, fitting into depressions in the bast-fibers, and that the outer walls are exceedingly thin, while the inner and side walls are strongly thickened,

[1] *De Palmarum Structura*, Translation in Ray Soc. Reports and Papers, 1849, p. 29.

[2] *Verhandl. d. Bot. Ver. Prov. Brandenburg*, Bd. xxiii, 1881, pp. 94–109.

thus bringing the cell cavity near the outer sufrace. Inclosed in each cell and filling it almost completely, is a silicious body, from ·006 to ·012 m.m. in diameter, with wart-like protuberances on the surface which fit into corresponding depressions in the cell walls (*Fig.* 7). That they are composed of silica is demonstrated by their incombustibility, their insolubility in hydrochloric and nitric acids and their complete solubility in hydrofluoric acid. Their appearance is particularly striking in tangential sections which have been heated on a cover glass until thoroughly carbonized and finally treated with hydrochloric acid on the slide. The heating

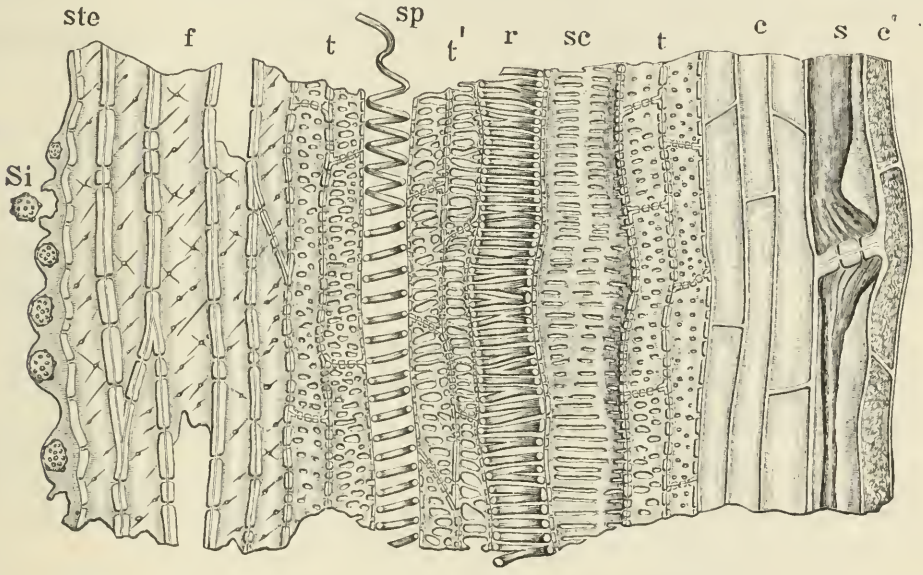

FIG. 6. Longitudinal section of a large (mesocarp) fiber of the cocoanut. *ste*, stegmata ; *Si*, silicious body ; *f*, bast fibers ; *t*, tracheids with small pits ; *t'*, tracheids with large pits ; *sp*, spiral trachea ; *r*, reticulated trachea ; *sc*, scalariform trachea ; *s*, sieve tube ; *c* and *c'*, cambiform cells. × 300.

should be performed at dull redness, since at a higher temperature the bodies lose their characteristic appearance.

Wiesner[1] refers to these stegmata as "bast parenchyma," and from his description it would appear that he considered them *silicified cells* and did not understand that they are *sclerenchymatized cells* with *silicious contents*. Von Hoehnel,[2] who uses, however, the term "stegmata," also appears to have fallen into the same error.

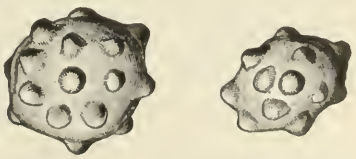

FIG. 7. Silicious bodies from the stegmata of cocoanut fiber. × 1500.

[1] *Loc. cit*, pp. 436–438.
[2] *Loc. cit.*, p. 52.

Rosanoff[1] found stegmata in twelve species of palms, and Kohl,[2] who has made an exhaustive study of the subject, in twenty-three additional species. Neither author mentions *Cocos nucifera*, but Kohl found in *C. flexuosa* stegmata with silicious contents which answer the description of those in coir fiber.

β. Bast-fibers (*Figs. 5* and *6, f*) completely surround the bundle. They vary in length up to 2 m.m. and in diameter up to ·03 m.m. The double cell walls are from one-half to one-sixth the breadth of the lumina, with conspicuous pores and diagonal markings. In longitudinal section the walls adjoining the stegmata are sinuous in outline, due to the depressions into which the stegmata are fitted. On the edge of the xylem the bast-fibers pass into tracheids (*Fig. 6, t*).

γ. Xylem (*Fig. 5, x; Fig. 6*). The elements are tracheæ, tracheids and various forms intermediate between tracheids and bast-fibers, and tracheids and parenchyma.

The tracheæ range in diameter up to ·05 m.m., the larger (found in large fibers) being reticulated (*Fig. 6, r*) or scalariform-reticulated (*sc*), the smaller (found both in large and small fibers) being spiral or reticulated spiral. Among the spiral tracheæ one finds considerable variation both as to their size and the steepness of their spirals. As might be expected, those in the protoxylem often have delicate spirals with turns wide apart. An intermediate form is shown in *Fig. 6* (*sp*).

The tracheids, distinguished from the tracheæ by the transverse or diagonal partitions and by their smaller size and thinner walls, likewise display an interesting diversity of size and form. Among these are forms with large pits and curious reticulations (*Fig. 6, t'*) also transitional forms between tracheids and bast-fibers (*t*) on the one hand, and tracheids and parenchyma on the other.

δ Phloem. Sieve tubes and cambiform cells make up the phloem (*Fig. 5, ph*).

Measured in cross sections, the diameters of the sieve tubes vary up to ·03 m.m. In longitudinal sections it may be seen that the sieve plates are either at right angles to the walls or oblique and that oftentimes they are covered with callus through which run a few indistinct pores (*Fig. 6, s*).

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[1] *Bot. Ztg.*, 1871, p. 749.

[2] *Kalksalze und Kieselsäure in der Pflanze, Marburg*, 1889, p 289.

Cambiform cells occur singly, in rows and in groups among the sieve tubes and also at the edges of the phloem. Those among the sieve tubes are for the most part small (about ·003 m.m. in diameter), prismatic and with abundant protoplasmic contents (*Fig. 6, c*[1]). They correspond to the "*geleitzellen*" of Wilhelm, Tschirch[1] and other authors except that the walls adjoining the sieve tubes, so far as the writer has observed, are not pitted.

At the edges of the phloem, particularly adjoining the xylem, the cambiform cells are larger (often ·01 m.m. in diameter) and are often empty. The differences between these forms are, however, so slight and perplexing that the writer, following the example of De Bary and Strassburger, prefers to group them all under the head of cambiform cells.

(*e*) Intercellular spaces, such as occur in the protoxylem of many monocotyledinous plants, are seldom, if ever, seen in coir fibers, but oftentimes, although less commonly than in the hard shell, the phloem and part of the xylem are destroyed during growth, leaving a channel in the bundle.

3. *Endocarp.*

This coat, known commonly as the shell (*Fig. 8, end*), is a dense aggregation of stone cells, among which run longitudinally partially destroyed bundles.

(*a*) *The stone cells* with their thick, deep yellow walls, branching pores, the dark brown contents, present a striking and characteristic appearance. They are either isodiametric or strongly elongated, the latter (often 0·2 m.m. long) being usually spindle or wedged-shaped, although hammer-shaped, hooked and various other curious forms abound.

A study of sections show that the elongated cells are arranged in groups, commonly with the longer diameters in tangential-transverse directions and are best seen in cross sections of the shell (*Fig. 8, qst*), but in some groups, particularly those adjoining the bundles, they pass longitudinally about the shell (*Fig. 9, lst*). It is evident from *Fig. 8* that more than half of all the stone cells are tangentially-transversely elongated. Those which appear isodiametric (*lst*) are partly cells which are isodiametric in three dimensions and partly longitudinally elongated cells in section.

[1] See *Tschirsch, Angewandte Pflanzenanatomie*, Wien, 1889, p. 349.

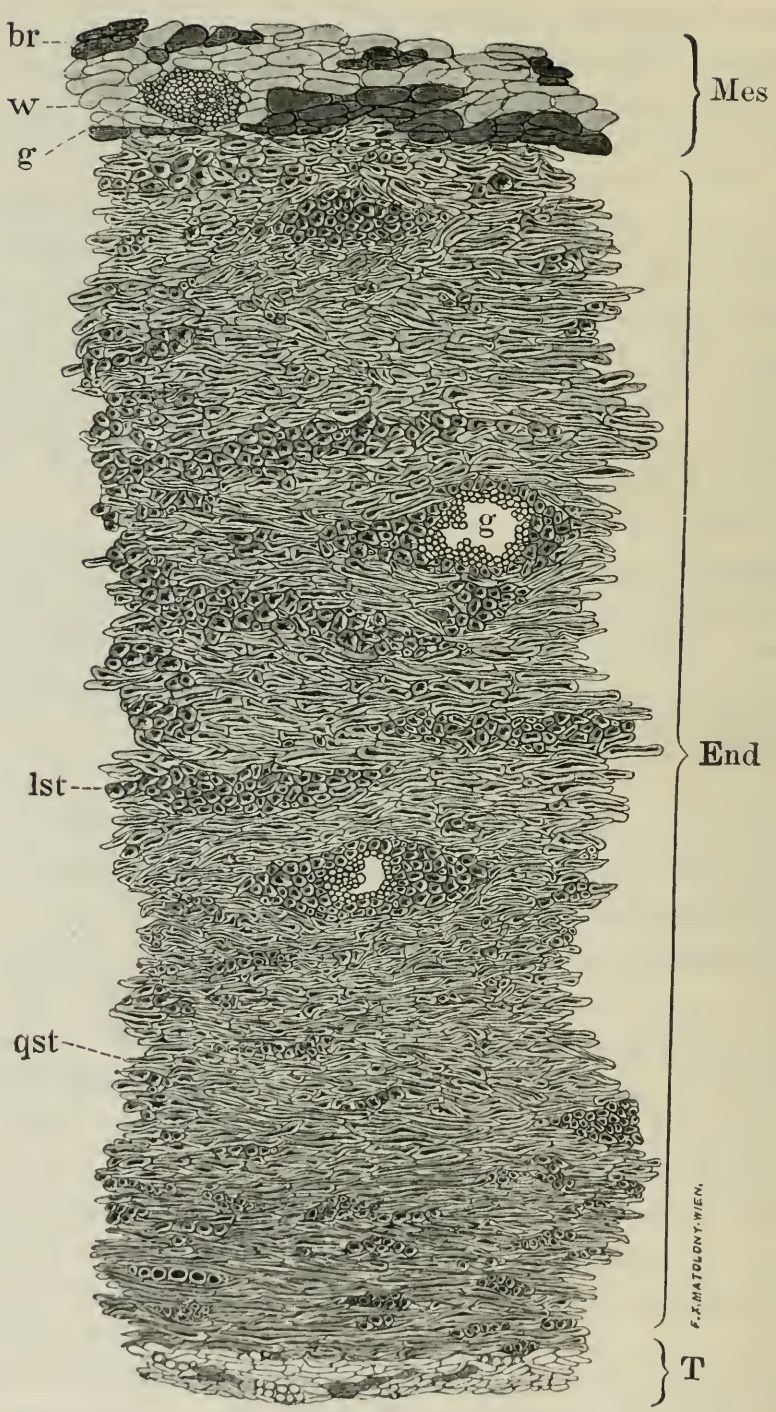

FIG. 8. Transverse section of a cocoanut shell. *End*, endocarp or hard shell; *Mes*, adhering mesocarp; *T*, adhering outer testa; *w*, colorless parenchyma of mesocarp ground tissue; *br*, same as *w* but impregnated with a brown substance; *g*, vascular bundles, in the endocarp with phloem and xylem partially obliterated; *lst*, longitudinally elongated and isodiametric stone cells; *qst*, transversely-elongated stone cells. × 60.

Groups of thinner-walled cells with dark brown contents are occasionally met with.

The brown contents of all the endocarp cells react the same as the brown impregnating material of the mesocarp.

(*b*) *Vascular bundles* are studied with difficulty in the mature shell. By the rupture of the phloem and part of the xylem during growth, passages are formed, which, in shells transversely cut or

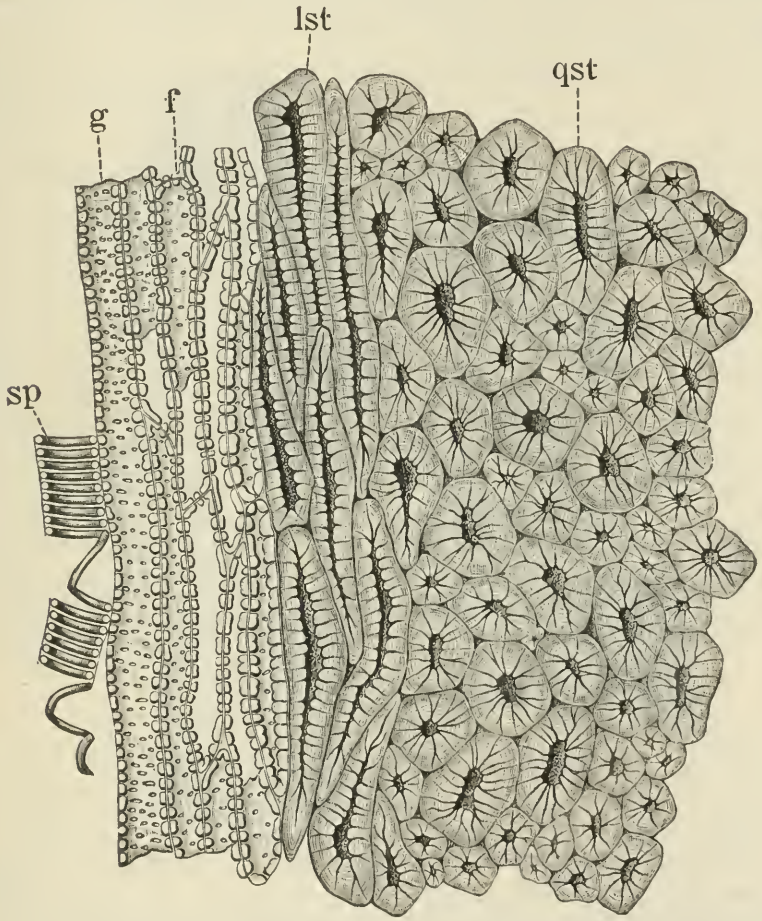

FIG. 9. Longitudinal-radial section of cocoanut endocarp through the stone cells and edge of bundle. *qst*, transversely elongated and isodiametric stone cells; *lst*, longitudinally elongated stone cells; *f*, thick-walled porous cells; *g*, pitted trachea; *sp*, spiral trachea. × 300

broken, are evident to the naked eye as minute holes. The structure of the bundles is still further obscured by the presence of fungus threads and spores.

In structure the bundles differ from those of the mesocarp fiber the bast-fibers being replaced by forms intermediate between fibers and tracheids (*Fig*, 9, *f*). The vascular elements are chiefly spiral

tracheæ (*sp.*), and pitted tracheæ (*g*), the latter being especially noticeable.

4. *Testa.*

Several microscopists have studied the testa, but, owing doubtless to differences in the material, hardly two of them agree as to the number of coats or the character of the elements. The description which follows is based on the examination of numerous specimens.

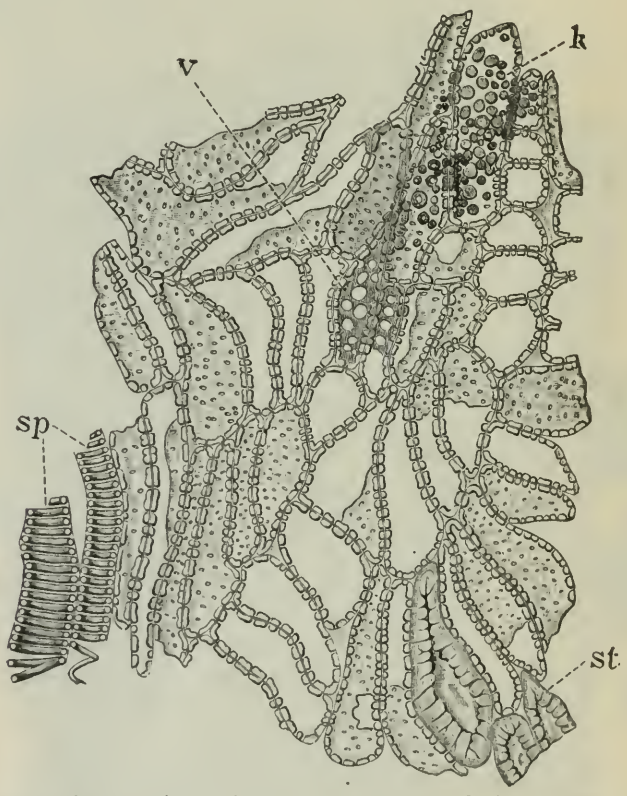

FIG. 10. Tangential section of the outer testa of the cocoanut showing the ground tissue of thick-walled porous cells. Most of these are empty, but a few contain brown contents in the form of globules, (*k*) or films with circular openings (*v*). *st*, colorless stone cell; *sp*, spiral trachea. × 300.

(*a*) *Outer testa.* This coat consists of a ground tissue of large, variously shaped cells, crossing one another in all directions (*Fig. 8, T, Fig. 10*), between which ramify the veins.

Most of the ground tissue cells have colorless double walls, from ·004 to ·010 m.m. thick, with conspicuous (sometimes large) pores, but in the inner layers they often have thinner walls without evident pores and except for their shape bear no resemblance to the other cells.

As a rule, the cells are empty, but some here and there contain a brown substance apparently the same as is contained in the mesocarp and endocarp, which often takes the form of spheres (*Fig. 10, k*), disks, or films with circular openings (*v*).

Colorless stone cells (*Fig. 10, st*) are present in the outer layers and contrast strikingly with the deep yellow stone cells of the endocarp.

The conspicuous elements of the veins are spiral tracheæ, pitted tracheæ and elongated cells intermediate between pitted tracheæ and the porous cells of the ground tissue, and are not distinguishable from the same elements of the endocarp bundles. (See *Fig. 9, sp, g* and *f.*)

In breaking away the meat, the separation is through the middle of the veins and the inner layers of the outer testa, nearly all the ground tissue and about half of the vascular elements remaining on the inner surface of the shell.

(*b*) *Inner testa.* Firmly attached to the endosperm are from ten to twenty layers of small isodiametric or slightly elongated cells. The double walls are about ·003 m.m. thick and free from pores. These cells contain a material varying in color from light yellow to dark brown, which either fills them completely or occurs in globules, films, etc., as in some of the cells of the outer testa. In the layer adjoining the endosperm the cells are smaller and have darker brown contents than the cells in the other layers.

5. *Endosperm.*

Although the microscopic character of the endosperm has been fully explained by Harz, Hanausek and Moeller, a brief description is here given to accompany the descriptions of the other parts of the fruit.

In the outer layers the prismatic cells are nearly isodiametric (about ·05 m.m. in diameter), but further inward they are radially elongated, often reaching a length of ·3 m.m. Cell partitions are about ·003 m.m. thick, without pores.

The cells contain bundles of needle-shaped fat crystals and lumps of proteid matter, each lump containing, as a rule, a crystalloid. Ether and alcohol readily dissolve the fat crystals and strong potassium hydrate solution saponifies them. The proteid bodies give the usual color reactions with iodine, Millon's reagent and dyes.

III. THE DETECTION OF POWDERED COCOANUT SHELLS IN GROUND SPICES.

The adulteration of ground spices with powdered cocoanut shells was brought to notice in 1885 by W. H. Ellis,[1] public analyst, Toronto, Canada, and has since been frequently detected by A. McGill[2] of Ottawa and food analysts in different parts of the United States.

The extent to which this fraud is practiced is indicated by the following summary of results obtained by the writer during the years 1896–7 in the examination of samples collected in the State of Connecticut.

	Black pepper.	Cloves.	Allspice.
Samples examined	147	37	24
Samples adulterated (total)	47	17	11
Samples adulterated with ground cocoanut shells,	21	7	6

It is stated on credible authority that in Philadelphia at the present time about six hundred tons of shells, obtained as a by-product in the preparation of dessicated cocoanut—an article much used in pastries and confectionery—are annually reduced to a powder in mills of peculiar construction and sold to spice grinders. This powder, without further treatment, is mixed with ground allspice, which it closely resembles in appearance. By cautious roasting the color of ground cloves and nutmegs is matched, and by roasting at a higher temperature a charcoal is obtained which, mixed with starchy matter, is a clever imitation of black pepper.

Powdered cocoanut shells appears to be a distinctively American adulterant. The leading treatises on the microscopy of foods in the German, French and English languages, even those of recent publication, make no mention of it, and a number of prominent European food chemists and microscopists have declared to the writer that they had never heard of its use. On the other hand, cocoanut cake (the residue from the oil presses), which in Europe is commonly employed, both as a cattle food and as an adulterant of human foods, is almost unknown in America.

All the tissue elements of the mesocarp, the endocarp and the

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[1] *Dept. Inland Revenue, Rep. on Adult. of Food for 1885*, Ottawa, 1886, pp. 67, 79.

[2] *Laboratory of the Inland Rev. Dept.*, Bull. No. 20, 1890, pp. 7–11.

outer testa are present in cocoanut shell powder, but the stone cells of the endocarp make up the bulk of the material. (*Fig. 11, st*). These cells are characterized by their porous, brown-yellow cell walls, their dark brown contents which become a reddish brown on treatment with potassium hydrate solution, and the predominance of peculiar elongated forms. They differ in one or more of these characteristics from the stone cells of pepper, allspice, clove stems, walnut shells, almond shells, Brazil-nut shells, hazel-nut shells, peach stones and olive stones.

The outer testa, or lining of the shell, also forms a considerable part of the powder, the most striking elements being the thick-walled, porous cells (*p*) and the vascular elements.

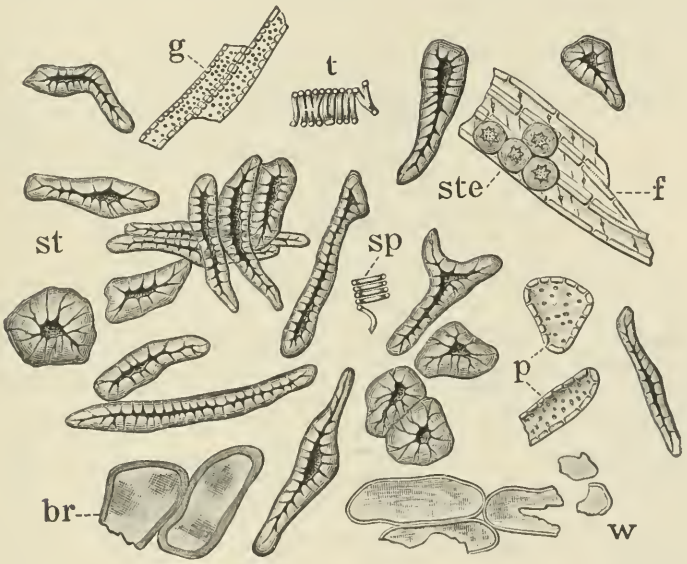

FIG. 11. Cocoanut shell powder. *st*, dark yellow stone cells with brown contents; *t*, reticulated trachea; *sp*, spiral trachea; *g*, pitted trachea; *w*, colorless and *br*, brown parenchyma of mesocarp; *f*, bast-fibers with stegmata (*ste*). × 160.

Colorless cells of the mesocarp ground tissue (*w*) are not distinguishable from the parenchyma of many other plants, but when impregnated with the brown substance which has been described they are striking objects (*br*). Potassium hydrate changes the color of these brown cells to a reddish brown, but ferric chloride does not produce any immediate effect, thus distinguishing them from cells of allspice seed, the color of which potassium hydrate removes and ferric chloride changes at once to a green.

Spiral, reticulated, and pitted tracheæ (*sp*, *t* and *g*), from the mesocarp, endocarp and testa bundles, are also frequently met with

in the powder, the pitted trachea being quite unlike any vascular elements of the spices.

The stegmata (*ste*) of the mesocarp fibers with their silicious contents are characteristic, but they are difficult to find owing to the great preponderance of other tissues. Bast-fibers (*f*) are more liable to be encountered than the stegmata, but they furnish less conclusive evidence.

Spices adulterated with charred cocoanut shells show under the microscope black, opaque fragments which are not bleached by aqua regia or nitric acid and potassium chlorate. Except in cases where some of the stone cells or other elements have escaped charring, this material cannot be distinguished from other forms of charcoal.

	Black Pepper. (Av. of 14 Analyses.)	Cloves. (Av. of 8 Analyses).	Allspice. (Av. of 3 Analyses.)	Nutmeg. (Av. of 3 Analyses.)	Cocoanut Shells. (1 Analysis.)
	Per Cent.	Per Cent.	Per Cent.	Per Cent.	Per Cent.
Water	11·96	7·81	9·78	3·63	*7·36*
Total ash	4·76	5·92	4·47	2·28	*0·54*
Ash soluble in water	2·54	3·58	2·47	0·86	*0·50*
Ash insoluble in hydrochloric acid	0·47	0·06	0·03	0·00	*0·00*
Volatile ether-extract	1·14	19·18	4·05	3·02	*0·00*
Non-volatile ether-extract	8·42	6·49	5·84	36·70	*0·25*
Alcohol extract	9·62	14·87	11·97	10·77	*1·12*
Reducing matters by direct inversion calc. as starch	38·63	8·99	18·03	25·56	*20·88*
Starch by diastase method	34·15	2·74	3·04	23·72	*0·73*
Crude fiber	13·06	8·10	22·39	2·51	*56·19*
Total nitrogen	2·26	0·99	0·92	1·08	*0·18*
Oxygen absorbed by aqueous extract	—	2·33	1·24	—	*0·23*
Quercitannic acid equivalent to O. absorbed	—	18·19	9 71	—	*1·82*

Chemical analysis is a valuable adjunct to the microscopic examination and often determines approximately the extent of the adulteration, but since other nut shells have a similar composition, the microscope is essential for the identification of the particular adulterant present. As was pointed out by the writer[1] five years

[1] *Conn. Agr. Expt. Sta.*, Rep. 1896, p. 34.

ago, the crude fiber obtained in the process of analysis is particularly suited for the microscopic detection of stone cells and other tissues.

The radical difference in composition between cocoanut shells and the spices to which they are added is shown by the results in the table on the preceding page by Winton, Ogden and Mitchell.[1]

In conclusion, the author takes this opportunity to thank his highly esteemed instructor, Prof. Dr. Josef Moeller of Graz University, Austria, for kindly assistance in the early part of this investigation. The work was begun in Professor Moeller's laboratory during the autumn of 1899, but after a year's interruption was finished at this station.

Acknowledgment is also due Prof. E. Gale of Mangonia, Florida, who generously furnished material for study, and also Herr F. X. Matalony, of Vienna, who skillfully reproduced on wood the author's drawings.

LABORATORY NOTES.

By Robert C. Pursel and Willard R. Graham.

Jaborandi Leaves.—The standard for the alkaloidal content of Jaborandi leaves has been set by the majority of manufacturers at 0·35 per cent. acid titration. During the past year nearly all of the samples submitted, answered the above requirement. Several samples, however, did not, as may be seen by the following data:

Six samples assayed between 0·17 and 0·28 per cent. of alkaloids, the average being 0·24 per cent.

All of the other samples contained a great many stems. The latter, when separated from the leaves of sample No. 5, were found to amount to 23·83 per cent.

Hydrastis Canadensis.—Several samples of golden seal were assayed, ether being employed in each case to dissolve the hydrastine, with the following results:

Five samples yielded between 2·76 and 4·16 per cent. of hydrastine by weight, the average being 3·47 per cent.

Carthagena Ipecac.—The following assays of Carthagena Ipecac tend to show that it is equal, if not superior, to the Rio variety in alkaloidal contents.

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[1] *Ibid.*, Rep. 1898, pp. 198–211.

Nineteen samples gave between 1·92 and 2·36 per cent. of total alkaloids in fresh drug, or calculated on moisture-free drug between 2·19 and 2·54 per cent.

Glycerin.—Several carloads of glycerin, obtained from one of the largest manufacturers in the country, have been examined recently. Aside from the trace of fatty acids it contained, it answered the U.S.P. requirements. It answered the U.S.P. tests for sugars, but when allowed to stand longer than six hours (from twelve to sixteen hours in the cold), it reduced Fehling's solution. For pharmaceutical purposes this probably would not be detrimental, but when used for preparing certain test-solutions that are in turn used for the detection of sugar in urine, the results might be very unsatisfactory for all parties concerned.

Soluble Blue.—Several samples of soluble blue were offered at a price much lower than we had been paying. Upon examination it was found to consist almost entirely of ultramarine blue, only a small per cent. being soluble. As there is a difference of about 25 cents per pound between the two (ultramarine being the cheaper) these parties, if they could have sold enough of their products, would, in a short time, have been millionaires.

Belladonna Leaves.—We have several times heretofore reported the alkaloidal content of belladonna leaves to be above the standard (*i. e.*, 0·35 per cent. total alkaloids by acid titration) adopted by manufacturers whose drugs are bought and sold upon the assay. Recently several samples were offered for sale and upon being assayed, they were found to be away below the standard. In appearance the leaves were very fine.

The analysis of nine samples gave between 0·10 and 0·22 per cent. of total alkaloids by acid titration, the average being 0·13 per cent.

Tannin Commercial.—A sample of tannin commercial was offered for sale at 35 cents per pound. As this was an exceedingly low price for this product, our suspicions were at once aroused and upon being assayed, it was found to contain 57·80 per cent. of tannin. In appearance it resembled finely powdered nut galls; this conclusion was confirmed by the per cent. of tannin it contained.

Yellow Wax.—Quite a few of the samples of yellow wax examined during the past year have been found to be adulterated in one way or another. The following table of constants shows the variations in the different samples:

No. of Sample	Specific Gravity at 15° C.	Melting Point.	Acid Value.	Saponification Value.	Ester Value.	Adulterant.
1	0·9437	62° C.	13·74	59.48	45·74	Paraffin.
2	0·9120	61° C.	10·77	56·78	46·01	"
3	0·9340	65° C.	6·36	30·72	24·36	"
4	0·9548	63·5° C.	19·16	99·92	80·76	
5	0·9560	63·5° C.	19·11	95·53	76·42	
6	0·9483	64° C.	27·14	102·36	75·22	Stearic acid paraffin.
7	0·9463	63° C.	24·31	95·00	70·69	" " "
8	0·9540	64° C.	19·50	93·33	73·80	
9	0·9520	52° C.	14·62	70·86	56·24	Paraffin, tallow, yellow ochre.
10	0·9515	63·5° C.	24·20	97·12	79·92	Stearic acid.

As may readily be seen by the above table, several samples are abnormal. When paraffin is used the acid value is naturally reduced; the latter is then brought up by the addition of stearin; usually in this case, too much is added, which makes the acid value abnormally high.

Laboratory of Smith, Kline & French Co.
Philadelphia.

SOME NOTES ON OLIVE OIL.[1]

By C. F. G. Meyer, Jr.

The olive tree is believed by some to be indigenous to Asia and the seeds, being carried by migratory birds to the Mediterranean regions, grew into a wild tree called the oliaster, having a kind of thorn and short leaves and producing but a very small berry. This variety has been carefully cultivated and is now known as the sativa, which has a lanceolated leaf and bears a larger fruit.

The olive tree prospers best in a calcareous, gravelly and dry soil on precipitous slopes which could be used for no other fruit-bearing trees. It is a fruit tree of the highest order, but a great deal of care must be given it in order to obtain the best results.

[1] [The above article by Mr. Meyer was prepared at the request of Joseph L. Lemberger, Ph.M., of Lebanon, Pa., who communicated the same to this Journal.—Editor.]

The average life of an olive tree is about one hundred years, but it may continue to bear fruit for a great many years after that age. It attains its full bearing capacity at about forty years, so that he who plants the tree does so more for posterity than for his own use, hence the old Tuscan proverb, *Vite di mio padre, olive di mio nonno*, which, freely translated, means, "The vineyard from my father; the olive yard from my grandfather."

When the tree has reached its maturity it is about 25 feet in height, has a very large trunk with widespreading branches, and small white flowers which grow in clusters, giving the tree a most beautiful appearance during the early spring months.

THE OLIVE AND ITS HARVEST.

The olives which are intended for preserving are picked early in September while they are still green, while those which are intended for oil are left until November, or even until the following year, by which time they have turned from a light green to an almost black color.

The oil pressed from the olives gathered in midwinter is preferred on account of its keeping properties; but the reason for an early harvest is that the insects have less chance to propagate in the fruit and that the new shoots which are to bear fruit the following year have not started and are thus safe from all injury.

The critical period of the olive is during the month of October when the fruit changes color, as in event of heavy rains or strong winds it is liable to be seriously damaged and it is therefore necessary to have experienced men constantly looking after the olive trees and to gather the nearly ripe fruit to prevent its being affected by these causes.

In former years the crops were gathered by women and children, who carelessly knocked down the fruit with long poles and in that way seriously damaged the berries so that they were unfit for making the finer grades of olive oil.

Nowadays, the olives are harvested by experienced men assisted by women and children. At first the ground around the tree is covered with large sheets of muslin to prevent the olive from being bruised when falling to the ground, as well as to protect them from the dirt which would greatly diminish the quality of the oil produced. The trees are then carefully shaken to bring down the ripe fruit.

After this shaking there are still some olives remaining on the tree. These are either hand-picked or are knocked down by gently tapping the branches with a long pole. When the fruit is all down it is gathered into large bags in which it is carried to the mill.

THE MILLS USED IN GRINDING THE FRUIT.

The mills in use today for the crushing of olives are very similar to those used for many centuries. One of the largest oil mills, situated in the suburbs of Nice, France, and which has been in possession of the family of the present owner for a great many years, is still being used with perfect satisfaction.

THE GRINDING OF THE OLIVES.

The olives are thrown into large stone crushers very similar to the chasers today used by the spice millers, with beveled edged millstones to fit the concave bottom of the container. The millstones are attached to a horizontal bar erected in the centre of the bowl, and it is by means of this bar that the stones are revolved. Some mills are operated by steam power, but more certain and satisfactory results are obtained by animal power, which is generally used, as the olives require slow and careful handling.

The millstones can be regulated so as not to crush the stone but simply to reduce the fruit to a paste-like substance.

After this has been accomplished the paste is transferred to flattish round bags loosely woven of grass and in which it is taken to the presses. These bags are so constructed that they will allow none of the pulp but only the oil to pass through them.

THE PRESSES AND HOW THEY ARE USED.

These bags are then placed on wooden platters of a trifle larger diameter, having handles on both sides, and are thus placed under the presses which are manipulated on very much the same order as our modern cider presses. The oil is forced out of the bags and caught up by drains which lead into large vats. Warm water is often poured through the presses so as to assist the flow of the oil, and when it reaches the vat the oil can easily be skimmed off of the water.

QUALITY IS THE MOST IMPORTANT FACTOR.

The finest quality of olive oil is that obtained from the first pressing and this is known as the (*olio di polpa*) pulp oil, or "Virgin oil," and contains nothing but the pure juice of the olive.

This oil is used for table purposes only, while that obtained from subsequent pressings of the residue, and which is a very inferior oil, is used in making soaps, liniments and lubricants.

The refuse which remains after the oil has all been extracted is used as a fuel or for manuring purposes.

THE ADULTERATION AND PRESERVATION OF OLIVE OIL.

Fraud is often practiced in the manufacture of olive oil, by taking olives which are not of a prime quality, or which have become mouldy, and adding leaves of the olive tree or seed oil to the pulp while it is being ground. These blend perfectly with the oil.

To keep olive oil in good condition the clear oil must be separated from the turbid at once, for the longer it remains in the lees the more apt it is to become rancid, as it absorbs oxygen rapidly and will soon reach a condition unfit for food. The original state can, however, be restored, as a general rule, by washing the oil with alcohol, or by using lime water in equal proportions. It congeals very easily when exposed to a low temperature, but by applying a little heat it will return to its original liquid state.

VARIETIES AND TESTS OF OLIVE OIL.

Olive oil varies greatly according to its physical characteristics, the finer quality, or "Virgin oil," having a pale yellow color with a slightly greenish tinge and only a very delicate odor, while inferior qualities have a more pronounced greenish color, a very unpleasant odor and a decidedly acrid taste.

The specific gravity of olive oil varies from 0·915 to 0·918 at 15° C. When heated to about 120° it becomes lighter in color; at 220° it is almost colorless, and at 315° it boils and produces a very disagreeable, rancid odor.

One of the principal adulterants is cottonseed oil, but rape oil is also used to a very large extent. Olive oil is slightly soluble in alcohol and dissolves very readily in ether, chloroform or carbon-disulphide.

One of the best tests for olive oil is the following, called—

BECHI'S TEST.

If 5 c.c. of the oil be thoroughly shaken in a test-tube with 5 c.c. of an alcoholic solution of silver nitrate (prepared by dissolving $\frac{1}{10}$

gramme of silver nitrate in 10 c.c. of deodorized alcohol and adding two drops of nitric acid to the mixture) and heated for about five minutes in a water-bath, the oil should retain its original color, not becoming reddish or brown, nor should any dark color be produced at the line of contact of the two liquids (absence of more than 5 per cent of cottonseed oil or any other foreign oils).

Another test for this oil is known as the "elaidin re-action," which is as follows:

If 10 c.c. of the oil be shaken frequently during two hours with a freshly prepared solution of 1 gramme of mercury in 3 c.c. of nitric acid a perfectly solid mass of a pale straw color will be obtained.

There are numerous other tests for olive oil but the above mentioned will give satisfactory results.

THE INFLUENCE OF CEREAL DECOCTIONS ON THE COAGULATION OF COWS' MILK.

By Charles H. La Wall.

For some years past it has been recognized by eminent authorities on dietetics that cereal decoctions, when added to cows' milk, play an important part in modifying the character of the curds which are formed when the casein is coagulated by the hydrochloric acid in the gastric juice.

The greatest difference between human milk and cows' milk has been shown to exist in the character of the curds which are formed by the addition of a coagulating agent; human milk forming fine flocculent coagula while cows' milk forms tough cheesy masses.

Many prominent pediatrists have long realized the value of cereal decoctions in the modification of cows' milk, and such men as Chapin, Heubner, Jacobi, Starr and Smith have openly advocated their use.

There has been some difference of opinion, however, as to whether conversion of the cereals has any modifying influence on the character of the curd, and this subject was taken up and thoroughly investigated by Dr. Franklin W. White about a year ago, with results which were summarized as follows:—

(1) Dilution of milk with cereal decoctions of proper strength renders the casein curd much more fine, soft and digestible than simple dilution with water. There is no difference in the action of various cereals, such as barley, oats, rice or wheat.

(2) The above property is due mainly, if not wholly, to the starch in solution, the most desirable amount of starch in the milk mixture for practical use is approximately three-fourths per cent.

(3) Diastase, by converting the starch to dextrine and maltose, promptly lessens and removes the action of cereal waters upon casein. Its addition, therefore, is not a practical measure when the action upon the curd is desired.

(4) Albumen water has no practical value as a diluent of milk.

(5) Lime water added to milk has no more effect than water upon the character of the curd produced in the animal stomach.—*Journal Boston Society of Medical Science*, December 4, 1900.

The following specimen tubes have been prepared in illustration of these facts:—

No. 1. Plain cows' milk, coagulated with HCl.

No. 2. Cows' milk and water (equal parts), coagulated with HCl.

No. 3. Cows' milk and cereal decoction, coagulated with HCl. Starch converted before coagulating.

No. 4. Cows' milk and cereal decoction (equal parts), coagulated with HCl. Starch converted after coagulating.

No. 5. Cows' milk and cereal decoction (equal parts), coagulated with HCl. Cereal decoction made from baked cereal flour.

No. 6. Cows' milk and cereal decoction (equal parts), coagulated with HCl. Cereal decoction made from arrowroot.

The curds in Nos. 1, 2 and 3 are seen to be in tough, cheesy masses, which would prove difficult of digestion even in the stomach of an adult.

The curds in Nos. 4, 5 and 6, on the contrary, are seen to occur in fine flocculent particles which would be easily attacked by the digestive enzymes.

The coagulation was accomplished by bringing the milk or milk mixture to a temperature of 100° F. and adding diluted HCl., several drops at a time, shaking after each addition, until the total acidity reaches 0·257 per cent, which is that of the normal human stomach.

The cereal decoctions were made by boiling the cereals for five minutes with water, regulating the amount so that the finished decoction contained 3 per cent. of starch.

NOTE ON SOUTHERN PRICKLY ASH BARK.

By W. L. Cliffe.

As is well known the Pharmacopœia recognizes two varieties of prickly ash bark; one being the product of Xanthoxylum Americanum, and the other Xanthoxylum Clava-Herculis, of which the

specimen I am enabled to present to the museum of this college through the courtesy of Mr. Robert Pursel, is a remarkably distinct example. In this part of the United States it has been the general custom to use the Northern, or X. Americanum, in the manufacture of pharmaceutical preparations; this selection being due, no doubt, to the fact that this variety is generally supplied by jobbers upon orders for "prickly ash bark."

There is a wide difference in the pharmacological value of the two barks; the southern or X. Clava-Hercules being far richer in the extractives which give the bark its medicinal value. As a practical illustration of this difference I have prepared two samples of the wine from typical specimens of each variety, and the color, pungency and bitterness are easily differentiated upon comparison. This difference is also readily noted upon chewing a portion of each variety. Another point noted in the manufacture of the wine, which is a 50 per cent. preparation, is that in the case of the northern variety a fairly good exhaustion of the drug is secured by good sherry, but in the case of the southern variety simply saturation occurs without thorough exhaustion, and the marc retains distinct identity.

Prickly ash has been prescribed frequently in Philadelphia as a uterine tonic and stimulant and also used externally as a counter-irritant and for all its therapeutic uses the southern prickly ash would seem to be more satisfactory than its northern relative.

PHILADELPHIA, October 15, 1901.

RECENT LITERATURE RELATING TO PHARMACY.

VALUATION OF NEW REMEDIES.

Professor Kobert, of Rostock, read a striking paper on the above subject at the German Naturalists' Convention (*Aerzt. Vereinsblatt für Deutsch.*, 1900, 435). He calls attention to the ever-increasing number of new remedies, their personal literature teeming with highly embellished testimonials, and withal how very little the practicing physician knows of their real value. He then asks if authoritative judgment of these remedies based on clinic, chemical and pharmacological examinations is possible, and how such judgment is best obtained.

The unsupported word of the medical press can be scarcely taken as their opinions are too strongly influenced by their advertising pages and reports of individual workers are of little value, as the finding of such data means search through a hundred journals.

What the practitioner needs is an authoritative publication relating to this subject and to this subject only, and entirely uninfluenced by advertisements.

How can this be accomplished?

The writer hopes to see the day when the paternal German government will establish an institute of medical testing, similar to the present Imperial Serum-Testing Institute, and like the pure food laboratories scattered throughout his country; that at this institute all new remedies be tested chemically, clinically and pharmacologically, and that only those medicaments receiving the approval of the institute be permitted sale in the empire.

That failing (or postponed) he suggests that the reform be inaugurated by the Naturalists' Society; that this association seek the aid of its members and others—pharmacologists, surgeons, gynecologists and other medical specialists, chemists, bacteriologists, etc., begging reports on each new medicine they have used. A committee is then to compile the data received and publish same for the benefit of the medical profession. It is assumed that physicians will then prescribe only those medicines recommended by the association—a rather doubtful assumption. H. V. Arny.

OVULA GLYCERINI.

For gynecological purposes, round suppositories containing about 16 grammes glycerin and appropriate medicaments are popular in France. The base of these are made, according to J. Hofmann, as follows: Fifty grammes gelatin is mixed with 100 grammes water and 250 grammes glycerin, warmed on water bath till dissolved and the water has evaporated, an addition 150 grammes glycerin added, as well as the medicating agent, and the melted mass poured into moulds and allowed to solidify.—*Ph. Weekbl.* through *Schw. Woch. f. Ch. u. Ph.*, 1901, 143. H. V. A.

CRYOSCOPY.

An interesting *résumé* of this study, which is destined to have pharmaceutical importance, is found in a paper by Ardin Delteil (*Schw. Woch. Ch. u. Ph.*, 1901, 195) in which the significance of

comparison of the freezing point of a solution with that of its solvent alone, is traced in historical order.

Raoult's law (depression of freezing point is directly proportioned to amount of solids dissolved); the discovery that equi-molecular solutions have the same depression of freezing point; the value of this fact in estimating molecular weights are all noted in the paper, but omitted here, as details can be found in any text-book on physical chemistry. In the paper particular stress is laid on the fact that depression of freezing point of a solution is in direct proportion to the osmotic pressure of same, hence by reading freezing point depression of a liquid, we learn its osmotic pressure. This measurement of osmotic pressure is of great value in physiological chemistry, and the estimation of depression of freezing point introduced by Dreser in 1891 has now become an essential part of the clinical examination of the liquids of the organism, such as blood, serum, urine, lymph, milk saliva, sweat, etc. It is interesting to note that all the physiological liquids save urine, have about the same freezing point depression (hence same osmotic pressure) as blood serum; that is, in the normal state of the organism, all its natural liquids are in physical equilibrium.

Cryoscopy is of interest to pharmacists inasmuch as the measurement of freezing point is becoming a necessary part of urine examination.

H. V. A.

SPURIOUS SANDARAC.

R. Haneke (*Pharm. J.*, 1900, p. 79), reports on a fictitious sandarac of Spanish origin. Physically it was an exceedingly fine specimen, consisting of elongated and rounded tears, pale lemon-yellow in color. On chewing, it adhered to the teeth, and melted at the temperature of the water bath, while sandarac is not materially changed at 130° C. (Some varieties of colophony possess as high a melting point as 135° C., L. F. K.). Sandarac has an acid number varying from 136–140. (The acid number of colophony varies from 130 to 181, L. F. K.). The above sample's acid number was 169. From the above date and etc., behavior towards solvents there is little doubt but that the specimen consisted of colophony.

L. F. Kebler.

FOOD VALUE OF EXTRACT OF MEAT.

L. Fürst, (*Chem. Ztg.*, 24, 994,) reviews the statement made by a number of authorities relative to the true nutritive constituents

of meat extracts and comes to the already generally accepted conclusion that the albumoses, peptones and albumins are present in too small quantities to serve of any value as foods. The small quantity usually taken can have nothing more than a stimulating effect. L. F. K.

PHENYLETHYL ALCOHOL IN ROSE OIL.

It has been the common experience of all investigators of steam distilled rose oil to find that it contained only a small percentage of phenylethyl alcohol as compared with the large percentage contained in extracted oils. (The steam oil is made from the fresh leaves, the extracted oil usually from dried leaves, L. F. K.) Walbaium came to the conclusion that this alcohol was not developed until the rose petals were dry. H. von Soden and W. Rojahn, *Ber. 33*, 3063, show that *the phenylethyl alcohol is quite soluble in the aqueous distillate and in this way is generally lost.* It can be extracted from the distilled water by shaking out with ether. These workers examined *rose pomade* made by the method of Hesse and Müller, *Ber.* 1899, *32*, 565 ; abstr. in Jour. Soc. Chem. Ind., *18*, 1899, 396) viz., macerating fresh rose leaves with warm fat, this pomade contained 0·56 per cent. of volatile oil; 46·5 per cent. of which was phenylethyl alcohol. "*Rose Pure*" a brownish yellow viscous oil, obtained by extracting the petals with a volatile solvent, was distilled with steam and the volatile oil thus obtained was found to contain 25 per cent. of phenylethyl alcohol. This investigation clearly shows that phenylethyl alcohol is a normal constituent of fresh rose leaves, being formerly lost in the aqueous distillate. See also this Journal, 1901, page 199. L. F. K.

OXIDATION OF ALOIN, BY MEANS OF POTASSIUM PERSULPHATE AND CARO'S ACID.

E. Seel (*Ber. 33*, 3212) found that the action of potassium persulphate on aloin from Barbadoes aloes produced different oxidation products, according to the quantity of reagent. An excess yields a pale-red compound, apparently an unstable oxygen addition product, in almost quantitative proportions. The same product is obtained by electrolytically oxidizing aloin in dilute sulphuric acid or by means of potassium percarbonate. Caro's reagent, sulphuric acid and potassium persulphate (*Ztsch. angew. Chem.*, 1898, 845);

or Baeyer's mixture of hydrogen peroxide and sulphuric acid (*Ber.*, *33*, 124), produce a brownish-red powder from which chloroform extracts tetrahydroxy-methyl-anthraquinone, $C_{15}H_{10}O_6$. L. F. K.

CITRAL, DETERMINATION IN OIL OF LEMON.

E. J. Parry, (*Ch. and Dr.* 57, 1900) replies to criticism contained in *Schimmel's Semi. Ann. Rept.*, October 1900, 25, on his method for estimating citral in lemon oil (*Chem. and Drug.*, *56*, 376). The first objection raised is that as high as 1 per cent. of citral passes over in distillations at very low pressures, this loss being made up or exceeded by the limonene absorbed by the cyanacetic acid solution. The second objection raised is that an exact reading of the volume in the graduated portion of a Herschsohn's flask is impossible. In reply to the first criticism the writer says that he has distilled many samples of lemon oil at a pressure of 10 millimetres and possibly below, but has never yet found any portion of the limonene to contain more than the merest trace of citral. The second objection is met by stating that the reading is not much more difficult than it is in several other absorption processes. He reiterates that his method gives more accurate results than any other thus far proposed. L. F. K.

MAIZE IN WHEATEN FLOWER, DETECTION OF.

E. J. Bevan tested (*Analyst*, *25*, 316). A. C. Wilson's method and found it to give satisfactory results. The process is executed as follows: mix the flour with clove oil and examine under the microscope with a one-fourth or one-eighth objective. The hilum of maize starch is indicated by a black dot or star while wheat and other starches are practically invisible.

G. Embrey (*Analyst*, *25*, 315) was unable to obtain satisfactory results with Baumann's quantitative method (*Ztsch. f. Untersuch. Nahr. u. Gemussmittel* 1899, *2*, *27*). He therefore offers the following modification: place 0·2 grammes of the sample into a 15 cm. by 2 cm. test tube, provided with a paraffined cork. Add 20 cc. of aqueous potassium hydroxide (18 Gm. per litre), shake well for three minutes, add twelve drops of 10 per cent hydrochloric acid, then introduce the tubes into a centrifugal and at whirl 600 revolutions per minute. Transfer 1 cc. of the clear liquid into a Neesler tube, dilute to 50 cc.; add 1 cc. of iodine solution (I, 0·25 Gm. KI, 1

Gm. and water to 250 cc.) and shake well, on comparing the tint obtained with the standard tints (made from known material) the percentage of adulteration can be ascertained within 5 per cent. A method for making more exact determinations is also given.

L. F. K.

QUANTITATIVE ESTIMATION OF FORMALDEHYDE.

After experimentation with all suggested methods of formaldehyde assay, Utz (*Süddtsch. Ap. Zt.*, 1901, 147) reports the following as satisfactory: *Henberg's* method, in which the sample is treated with an aqueous solution of diphenylen-dihydrazin hydrochlorate, and from the weight of the washed and dried crystals of composition,

$$\begin{array}{l} C_6H_4HN - N = CH_2 \\ \quad\quad\quad\

cally only in the starch-bearing parenchyma cells of the rhizome and the rootlets. The alkaloids are found most abundantly in the older parts of the rhizome, attaining the minimum at the root cap. The stem contains some alkaloid, also in the starch-bearing parenchyma, but the bulb scales and the leaves contain only traces. This is out of harmony with the previous investigations of Borcon, who claimed that the alkaloid was chiefly found in the cell walls of the epidermis—an error in judgment, due to the use of concentrated sulphuric acid as the reagent.—(Dr. Rinquist, *Ph. Post*, 1901, 117.)

H. V. A.

REVIEWS AND BIBLIOGRAPHICAL NOTICES.

Practical Text-Book of Plant Physiology. By Daniel Trembly Macdougal. With 149 illustrations. London and Bombay: Longmans, Green & Co.

This work is intended to bring together the facts and theories regarding plant physiology so that the student may profitably pursue such investigation. The author has not only drawn from his own resources but has obtained the fortunate coöperation of a number of well-known American botanists in the preparation of certain parts of the book. The following is a synopsis of the contents of the work: (1) Nature and relations of an organism; (2) relation of plants to mechanical forces; (3) influence of chemicals upon plants; (4) relation of plants to water; (5) relation of plants to gravitation; (6) relation of plants to temperature; (7) relation of plants to electricity and other forms of energy; (8) relation of plants to light; (9) composition of the body; (10) exchanges and movements of fluids, (11) nutritive metabolism; (12) respiration, fermentation, and digestion; (13) growth; (14) reproduction; (15) an appendix of tables; (16) an index.

It is extremely fortunate that the author has collaborated the results of the various investigators in physiological botany and brought them together in such a small volume. One of the most wholesome lessons to be learned from a careful perusal of the book is the extensive theorizing that is done in this branch of botany on more or less isolated experiments and the careful work that is necessary in order to develop the science of plant physiology. For instance, in the portion on "the influence of chemicals on the toxicity

of certain substances;" their retardation of plant growth is considered but no mention is made of the fact that these so-called toxic substances may not only possess an inhibitory effect on plant growth in one degree of concentration, but according to the varying strength of the solution they may simply retard development temporarily, or may stimulate activity or produce no effect whatsoever.

The Absolute Atomic Weights of the Chemical Elements, established upon the analyses of the chemists of the nineteenth century and demonstrating the unity of matter; presented in simple language to the general scientific public. By Gustavus Detlef Hinrichs. St. Louis, Mo.: C. G. Hinrichs.

This work is divided into four parts, in which are considered: (1) The errors of precision in atomic weight determinations; (2) the absolute atomic weight of ten leading elements; (3) the absolute atomic weights of boron and nitrogen; (4) tabular view of the atomic weight analyses of the nineteenth century.

The author shows the liability to error in taking the mean of a series of determinations as the basis of arriving at the true atomic weight of the elements. In the note on the atomic weight of arsenic (see this Journal, p. 497) the author has shown the precision of his method.

The diamond has been taken as the standard of matter for all atomic weight determinations, and the methods of direct oxidation and reduction of the metals as employed by Berzelius and his pupils are considered among the best methods for atomic weight determinations. The labors of the author are deserving of careful consideration. It is unfortunate, however, that he has not been content simply to discuss the labors of Stas, Clarke and others. While the language used in regard to various chemists may not vitiate the facts, it will, however, tend to prevent their dissemination as easily as otherwise might have been the case.

Die Serum-, Bakterientoxin- und Organ- Präparate. Ihre Darstellung, Wirkungsweise und Anwendung. Für Chemiker, Apotheker, Aerzte, Bakteriologen, etc., dargestellt von Dr. Max v. Waldheim. Wien, Pest, Leipzig: A. Hartleben's Verlag.

The remarkable discoveries in the past ten years in bacteriological, physiological and chemical researches under the leadership of Pasteur, Koch, Behring and others, has given us in blood serums, bacteria

toxins and organo-therapeutic preparations a remarkable class of remedial agents in disease. Most of these results have been published in the various journals or in special monographs. It is extremely satisfactory to have a work such as the present one of Dr. Waldheim containing all these different results so that one can familiarize oneself with these new preparations. The following subjects are treated in this book: In Part I: Alkoholismus; Blattern (variola vera); Cholera; Diphtherie; Dysenterie; Gelbfieber; Gonococceninfection; Kolibaccillose; Krebs (carcinoma) und Sarcom; Künstliche Sera, Medicamentöse Sera; Lepra; Lyssa, Tollwuth (rabies); Pest; Pneumonie; Pyocyaneusinfection; Reconvalescentenblutserum; Rhinosklerom; Schangenbissvergiftung; Staphyloccen-infection; Streptococceninfection; Syphilis; Tetanus; Tuberculose; Typhus. In Part II the following subjects relating to organo-therapeutics are considered: Blutbildungsorgane, embryonale; Blutegel; Bronchialdrüsen; Eierstock; Gehirn; Gehirnanhang; Hoden (Brown-Sequardine); Hornsubstanz; Knochenmark; Leber; Lunge; Milchdrüsen; Milz; Muskeln; Mutterkuchen; Nebennieren (glandulæ suprarenales). Nebenschilddrüsen; Nieren; Nukleinstoffe; Ohrspeicheldrüse; Pankreas; Schilddrüse; Schleimhäute.

An index arranged according to subjects and another according to authors completes this valuable little work. The cost of the book bound is 6 m., 80 ff.; in a paper cover, 6 m.

Die Technik der Kosmetik. Handbuk der Fabrikation, Verwerthung und Prüfung aller kosmetischen Stoffe und der kosmetischen Specialitäten. Von Dr. Theodor Koller. Wien, Pest, Leipzig: A. Hartleben's Verlag.

Inasmuch as the preparation of the various cosmetics is dependent upon the application of the principles of chemistry and bacteriology it is possible that this art may be developed as a branch of one of the applied sciences. The field is peculiarly fertile and attractive and those who are in any way interested in the subject will find the work of Koller of great value. The following is a list of contents: Die Aufgaben der Kosmetik; Materialienkunde (under which are given the various methods of preparations of odorous principles and the chemical, animal and plant substances employed); Allgemeine kosmetische Mittel (includes various preparations for the care of the teeth and hair); kosmetische specialitäten; Antiseptische

Wässer und Seifen; kosmetische Toiletteseifen und hygienische Seifen; kosmetische Geheimmittel; Prüfung und Untersuchung von in der kosmetischen Technik verwendten Stoffen.

The work contains numerous formulæ as well as the general consideration of the general principles involved in their preparation and application.

PHARMACEUTICAL MEETING.

The first of the series of pharmaceutical meetings of the Philadelphia College of Pharmacy for 1900–1901, was held on Tuesday, October 15. Prof. C. B. Lowe presided, and in opening the meeting stated that it was the desire of the committee having these meetings in charge to make the present series even more useful than their predecessors, presenting matters in particular relating to practical pharmacy, and urged all those present to co-operate in this work. The programme was an interesting one and the first speaker introduced was Dr. Jokichi Takamine, of New York City, who read a paper on "Adrenalin the Active Principle of the Suprarenal Glands and its Mode of Preparation." (See page 523.) The author stated that he had succeeded in isolating adrenalin in a pure, stable and crystalline form, which latter character he illustrated by means of diagrams. Several of the characteristic tests for the substance were carried out and also a diagram was exhibited showing the effect of the substance on the blood-pressure.

In the discussion on this subject Dr. Lowe spoke of the influence of the suprarenal glands on the vasomotor system and their usefulness in keeping up its tone. He said that until recently it had not been well understood just how this influence was exerted, but that now it was ascribed to adrenalin. He attributed its usefulness in inflammation to its power of reducing the calibre of the vessels and hence the amount of blood. In reply to a question by W. L. Cliffe as to the keeping qualities of the solution in which form adrenalin is generally sold, Dr. Takamine said that it might be compared to cocaine in this respect, and that certain chemicals, such as boric acid, are used to preserve the solutions. Sodium chloride is also added to the solution so as to render it non-irritating in eye and nose affections, this addition not being objectionable, particularly in disease of the heart. With regard to the activity of adrenalin the speaker stated that it was not poisonous and appeared to be

perfectly inert when administered to persons in normal condition, but when used with persons having a weak heart its effect was soon noticed.

M. I. Wilbert, of the German Hospital, Philadelphia, read a paper on "Digestive Ferments in Surgical Practice," and presented in connection therewith a sample of a physiological solvent which is in use at the Hospital and which he has designated as "Physol." (See page 535.)

W. L Cliffe presented a "Note on Southern Prickly Ash Bark," and on behalf of Mr. Robert Pursell donated a fine specimen of the drug to the college. (See page 562.)

Charles H. LaWall read a paper on "Coagulation of Cows' Milk by Cereal Decoctions," which subject he illustrated by means of a number of specimens. (See page 561.)

The next feature of the programme was an exhibition of specimens of the adulterations of drugs, submitted by the Smith, Kline & French Co. These specimens constituted the exhibit made by this company at the St. Louis meeting of the American Pharmaceutical Association, and were described by Lyman F. Kebler.

In connection with this subject Evan T. Ellis read a letter from a London firm to whom he had sent a quantity of peppermint oil, which he had purchased from an American house, stating that the oil contained 12·15 per cent. of resin and was of a reddish color. In remarking on this subject Mr. Kebler said that old oils were likely to contain resin, but that the amount reported was large. In regard to the color he said that it is quite common to find essential oils colored. This is due to the fact that if water be present in the oils, it separates out in cold weather and rusts the containers, thereby causing coloration of the oils.

Mr. LaWall exhibited a subliming vessel containing iodine, part of which was sublimed and the remainder in the crude condition, the sublimation having been carried on by means of the waste heat from a boiler.

Before adjournment the chairman announced that Mr. Henry P. Hynson, of Baltimore, would be present at the next meeting and present a paper on "Modern Drug Store Methods," and also that Mr. Wilbert would present a communication on a "Metric Medicine Glass."

FLORENCE YAPLE,
Secretary, pro tem.

PHILADELPHIA COLLEGE OF PHARMACY.

The semi-annual meeting of the members of the Philadelphia College of Pharmacy was held September 30, 1901, the President, Howard B. French, in the chair; thirty-five members were present. The minutes of the quarterly meeting held June 24th were read and approved. The minutes of the meeting of the Board of Trustees for June were read by the Registrar, W. Nelson Stem, and approved as read.

Mr. Stiles, for the delegates to the Pennsylvania Pharmaceutical Association meeting held at Harvey's Lake, June 18–21, reported verbally, as a very full report of that meeting had been published in the AMERICAN JOURNAL OF PHARMACY for September, page 446. Further report was unnecessary. In addition to what had already been published Professor Remington alluded to the good work that had been done by Joint Committees of the Pennsylvania Medical Association and Pennsylvania Pharmaceutical Association on free dispensaries and that the Medical Association at the meeting recently held in Philadelphia had unanimously adopted the plan proposed by the Joint Committee (see AMERICAN JOURNAL OF PHARMACY, page 467). Credit was due our fellow member, J. C. Perry, who was the author of the plan.

The report of the delegates to the American Pharmaceutical Association held at St. Louis, September 15–20, was read by Professor Kraemer, as an extended report of the proceedings was published in the AMERICAN JOURNAL OF PHARMACY for October, page 482–510, he called especial attention to the fact that as the next meeting will be held in Philadelphia in 1902 it would seem desirable to appoint a committee to consider in what way, or ways, the College might contribute to the success and interest of the meeting.

The suggestion was discussed by Messrs. Meyer, Lowe, Cliffe, Perry, Kraemer and Remington, when Professor Remington offered the following resolution: "That a committee of five be appointed by the chair to take into consideration all matters pertaining to the meeting of the American Pharmaceutical Association in 1902 in which the College may be 'interested,'" which was adopted, and the chairman be requested to appoint the committee at his leisure.

Mr. England, for the Committee on Nominations, reported that, in accordance with Article VIII, Section 19, the following named gentlemen were proposed for the three vacancies in the Board of Trustees, which would occur at this meeting of the College—E. M. Boring, R. M. Shoemaker, Lawson C. Funk, Charles Leedom and Walter A. Rumsey.

Election for three trustees being next in order, letters were read from Messrs. Funk and Rumsey declining the nomination. There being no further nominations, on motion of Mr. Gordon the Secretary was directed to cast an affirmative ballot for Messrs. E. M. Boring, Richard M. Shoemaker and Charles Leedom, for the term of three years. Melville W. Bamford and Lucien Scott Kemp were unanimously elected to membership in the College.

The President expressed his pleasure at the larger number of members present at the meeting.

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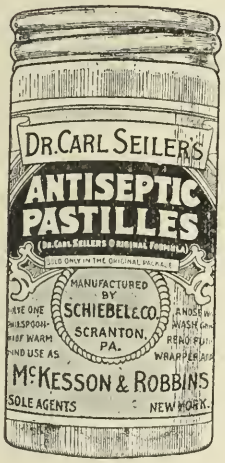
Missouri,	A. T. Fleischmann,	Sedalia.
Montana,	C. B. Hoskins,	Butte.
Nebraska,	N. P. Hansen,	Kearney.
Nevada,	F. J. Steinmetz,	Carson City.
New Hampshire,	G. F. Underhill,	Concord.
New Jersey,	H. A. Jorden,	Bridgeton.
New Mexico,	W. C. Porterfield,	Silver City.
New York, E. Branch,	Sidney Faber,	New York.
" " M. "	W. L. Bradt,	Albany.
" " W. "	George Reimann,	Buffalo.
North Carolina,	W. Simpson,	Raleigh.
North Dakota,	W. S. Parker,	Lisbon.
Ohio,	W. R. Ogier,	Columbus.
Oklahoma,	F. B. Lillie,	Guthrie.
Oregon,	G. C. Blakeley,	The Dalles.
Pennsylvania,	C. T. George,	Harrisburg.
Rhode Island,	H. A. Pearce,	Providence.
South Carolina,	M. H. Sandifer,	Rock Hill.
South Dakota,	E. C. Bent,	Dell Rapids.
Tennessee,	R. L. Eves,	Nashville.
Utah,	C. H. McCoy,	Salt Lake.
Vermont,	J. G. Bellrose,	Burlington.
Virginia,	T. A. Miller,	Richmond.
Washington,	P. Jensen,	Tacoma.
West Virginia,	W. S. Hamilton,	Fairmont.
Wisconsin,	E. B. Heimstreet,	Janesville.

IMPORTANT NOTICE

DR. CARL SEILER'S
ANTISEPTIC PASTILLES

Dr. Carl Seiler's Original Formula



Numerous attempts have been made by manufacturers to furnish a tablet which, when dissolved in water, would yield a solution similar to the famous Seiler's Solution. Such preparations as have been placed upon the market yield solutions which do not represent the original preparation, and in addition cause irritation and smarting when used in the nasal cavity. Dr. Carl Seiler has consequently been compelled to request manufacturers to withdraw his name from their preparations.

The correct formula has been given by Dr. Seiler to Messrs. Schiebel & Co., of Scranton, Pa., who alone are now authorized to manufacture and use the name "Dr. Carl Seiler's Antiseptic Pastilles."

Dr. Carl Seiler's Antiseptic Pastilles

are supplied to the trade solely by McKESSON & ROBBINS, in metal screw-top bottles, each containing 50 pastilles, as per illustration shown above.

PRICES ARE AS FOLLOWS:

Lots of 1 to 3 Dozen,	=	per dozen, $3.00
Lots of 3 Dozen at one time,	=	per dozen, 2.75
Lots of 12 Dozen at one time,	=	per dozen, 2.50

The trade is cautioned against spurious preparations, and against using the name of Dr. Carl Seiler upon any similar preparation

ABSOLUTE PERFUME ESSENCES

We are placing within easy reach of dealers an opportunity to manufacture, by very simple methods, high-class French perfumes, having all the beauty and intensity for which these compositions are remarkable. The leading odors made abroad, on which French houses are staking their reputation, can be exactly reproduced at low cost by means of these aromatic principles.

Absolute essences are supplied in quantities to suit purchasers. The following odors are carried in stock :

Violettes de Russie
Violettes d'Italie (green)
English Apple Blossoms
Carnation Pink
Lilas de France
White Arbutus
Heliotrope Blanc
Indian Hay
Trefle de l'Incarnat
Rose de la France
and
Peau d'Espagne

Write for price list and descriptive circular

LEHN & FINK

Manufacturing Perfumers NEW YORK

WYETH'S

PREPARED FOOD

FOR

Infants and Invalids

PREPARED FROM

MALT, MILK AND CEREALS

NEW SCIENTIFIC RELIABLE

A food formed to meet the conditions which these two phases of life present must be chemically and physiologically adapted; the nutritive elements must be fixed and concentrated; the assimilable properties must be so adjusted that there must be a quick absorption and appropriation, and there must be no excess of substance to tax the power of digestion.

The superior of mother's milk; a combination affording the physician every advantage and embodying the established principles of infant feeding and hygiene.

Its diastasic properties prevent curdling, correct the ills of malnutrition and tone the weak and wasted organs of digestion.

Wyeth's Prepared Food is not a predigested Food, but one that will digest itself under all conditions—the Malt, rich in diastase, acting in conjunction with the pancreatic secretions, digests the fats and albumenoids of the milk, converting the starch of the cereals into sugar (Maltose) and neutralizing the tendency of the acids of the stomach to form curds—thus rendering the Food of infinite value to the infant and invalid alike, supplying the necessary nutrition and material to strengthen and build up the human economy.

Its digestive properties may be shown by simple test, the progress of conversion being readily noticeable.

PUT UP IN GLASS CONTAINERS AS FOLLOWS:

In 8-oz. bottles, 35c. size, $2.80 per doz. In 16-oz. bottles, 65c. size, $5.20 per doz. Hospital size, 6 lbs., $2.00 per bottle

JOHN WYETH & BROTHER

INCORPORATED

PHILADELPHIA, PENNA., U. S. A.

Write for copy of "Prices Current" for 1900

Every Drug Ground by Us Botanically Correct

Those that depend upon alkaloids for their medicinal value are assayed and required to come up to

STANDARD STRENGTH

Every article not perfect in all respects is rejected.

The pharmacist is assured, when using our Powdered Drugs for percolation, that his preparations will be of proper strength and free from admixtures of false or foreign matter.

Send for Price List and Formulary.

GILPIN, LANGDON & CO.

BALTIMORE, MD.

Panopepton with Iron

Contains the ferruginous element in peculiar organic combination with the peptic proteoses as formed in the peptonisation of the food proteids of the Panopepton.

The iron is bound to the food substances in a manner that cannot be accomplished by extemporaneous admixture of iron with Panopepton.

PANOPEPTON WITH IRON is put up in the same size and style of package as Panopepton "plain" and sold at the same price, $8.50 per dozen.

Fairchild Bros. & Foster

NEW YORK